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NEUROTOXICITY OF CYCADS
AN ANNOTATED BIBLIOGRAPHY FOR THE YEARS 1829-1989
(Annotated)

MARJORIE GRANT WHITING

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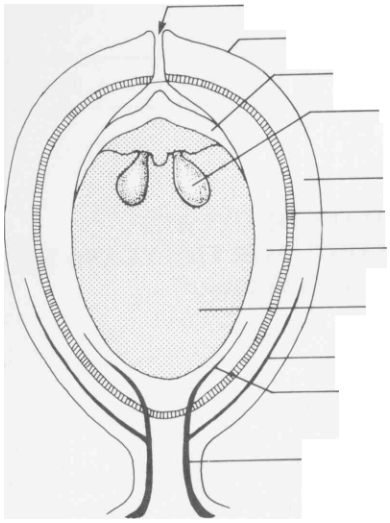
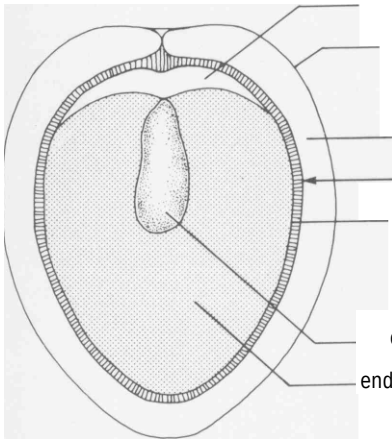




Top: Cycad ovule. *Bottom:* Cycad fruit and seed.

PREFACE

The living cycads are remnants of plants that were common on the earth throughout the Mesozoic and into the Paleozoic era. Fossil cycads are the extinct plants of the Mesozoic era.

All cycads are now listed in Appendix II of the CITES list of rare and endangered species. C. J. Chamberlin first published *The Living Cycads* in 1919 after studying all the genera for 15 years in the field and laboratory. The world map on page 8 shows the geographic range of the ten genera today.

Cycads are well known as decorative plants, particularly among the Japanese. The seeds and stems of all species contain an edible starch of good quality. This was not eaten by the Chamorros in Guam until after the Spanish taught them a safe method of preparation. Processing is long and tedious, and short cuts carelessly introduced may lead to illness and death.

This is an annotated bibliography of references to cycad toxicity. It provides a selection pertinent to the developing reputation of cycads for producing neurotoxic effects when fed or applied to man or beast. The references are arranged chronologically, dating from the earliest found (1829) to early 1989, thus providing a sequence of the evolution from hearsay to clear evidence and experimental studies.

Kisby et al. (1988) have described a rapid, sensitive, high-performance liquid chromatographic (HPLC) method for measuring beta-M-methylamino-L-alanine (BMAA), a naturally occurring amino acid present in cycad seeds that has been demonstrated experimentally to cause neurotoxic symptoms in primates. More recently (1989) Peter Spencer has described the growing concern in developing countries over the rising incidence of age-associated disorders, especially those involving the nervous system. Spencer writes of projections indicating that by the year 2050 the proportion of the U.S. population aged 65 and over will be almost double the 1981 level, while the prevalence of senile dementia of the Alzheimer type will triple in that time. In certain other parts of the world, however, notably the western Pacific, some of these disorders are even more common. Spencer suggests that these areas are more likely to provide opportunities for fruitful investigations.

ACKNOWLEDGEMENTS

In Appreciation: In preparing material for this bibliography, I am indebted to many, most of all Dr. Hilmer Frank, microbiologist, who took on the job of editing the final draft of the computer entries for the bibliography. With Iris Lee, his secretary, they completed the work in record time. We are grateful to both of them. Kristy Kiyonaga, an undergraduate during the school year, and Caroline Parker, completing her Master's Thesis this spring term, were both willing to learn, flexible, and amenable to new direction and frequent changes.

Sandy Shimabukuro, with her experience and knowledge about computers, gave us helpful advice on several occasions. A dozen or more librarians and language specialists at Hamilton Library, University of Hawaii, and at Guam University Library contributed their skills and knowledge. Chief among them is Mrs. Marjorie G. Driver, Director of the Micronesian Center at Guam University. During my brief visit in Guam this spring, her knowledge and experience were of great value to me. Dr. John Steele, who as he has commuted and communicated by fast plane and telephone, has shown us how to get the best service out of the East and West, out of Hawaii and Guam, the modern and the traditional.

I personally am grateful to Dr. Peter Spencer for his advice and support regarding the format and content of this volume. His contributions are notable. Dr. Yoneo Sagawa, Director of the Harold L. Lyon Arboretum at the University of Hawaii, has been patient and understanding concerning schedules and arrangements.

Many of those working on the project, not only in the 1950's but also in Guam and Hawaii in 1987 and 1988, have been volunteers with whatever skills they had to contribute. We extend our thanks.

We are most grateful to Mrs. Marty Rutan, who came from the mainland to Hawaii at her own expense, worked diligently at an early stage, and contributed of her skills with patience and intelligence on whatever job she was asked to do.

Ray Baker, in charge of the computer at the Lyon Arboretum, cheerfully rescued us from computer tangles that were not of his making, through his "hands-on" experience with both computers and cycads. Our families and friends helped keep our enthusiasm and morale at a high working level.

Marjorie Grant Whiting, Editor.
August, 1988

INTRODUCTION

For two years (1954-1956) my husband and I lived on the island of Ponape in the South Pacific. From the time I started to pack for our return home, casual friends and intimates asked what I planned to do with my big empty trunk. Well, I thought I might write a cookbook, and the empty trunk seemed a good place to file my collection of notes.

When I accidentally met Drs. Mulder and Kurland[1] in Guam, however, they proposed that I change my plans. As neurologists, they had studied the Chamorro population on Guam for several years for clues to the cause of the highest incidence in the world of amyotropic lateral sclerosis (ALS), also known as Lou Gehrig's disease. Genetics had not proven to be the answer, and the question of nonviral environmental factors had been raised. I accepted their proposal, agreeing to stay two months to study the diet of the local Chamorros. It was decided that I should live in Umatac for the first month, then with a family in Yigo for the second month. My search would focus on native plants used for food and/or medicine that might have neurotoxic effects. Larry Iriate, then a medical assistant and now superintendent of the Saipan Hospital, arranged the logistics.

The Chamorro culture was new to me. After a survey of food practices in normal times, it seemed important that we should explore the variations when food supplies were scarce, as in wartime or after typhoons. I suspected that low-prestige foods and those of questionable safety would be held for an emergency. I am not a botanist and had never heard of cycads, so I had a great deal to learn.

Wherever I visited, I helped with the food preparation and participated in celebrations from christenings to funerals. Food for a communal meal was usually prepared at night in one household by a dozen or more women, with plenty of gossip and laughter until nearly dawn, while the men went fishing. Much of the talk was in Chamorro, and while I didn't understand the words, I appreciated the spirit. By midmorning all was ready, including the fish, and we waited impatiently for the priest to come and ask the blessing, for these were usually religious occasions.

People were hospitable and friendly. Often a small child would come by to invite me to lunch because his mother had prepared a special Chamorro dish. I did prefer this to a Spam sandwich and a coke, the usual fare for a foreign visitor.

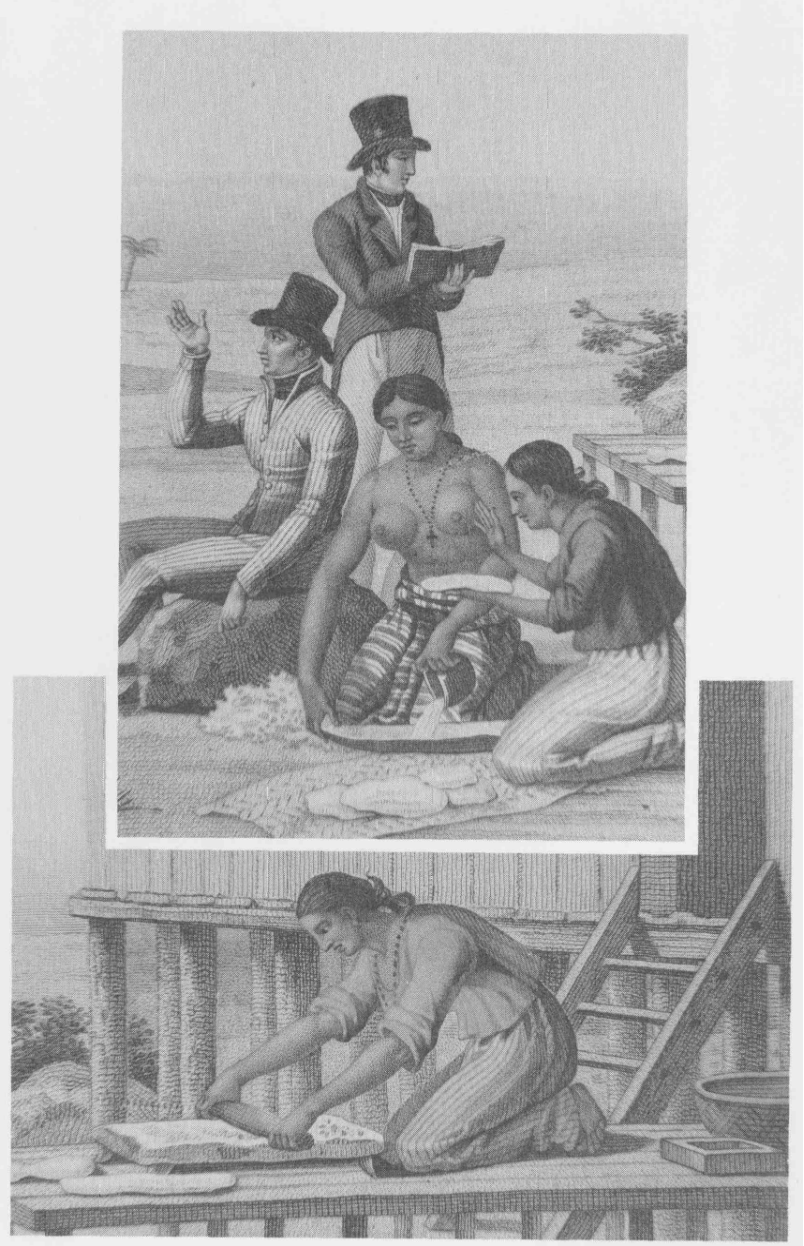
Although my search was fascinating, I was not always certain whether the stories I heard were fact or fiction. I made copious notes; my trunk was beginning to fill up. For example, I was told by a local man that the first he knew of "lytiko" (short for "paralytiko", many cases of which are diagnosed as ALS) was on a night when he was returning from fishing. As he walked across the flats, he felt a chill and a cold breeze on his chest and upper arms. He was frightened, but he did not see the doctor or tell any-

[1] Drs. Donald Mulder and Leonard Kurland, both from the Mayo Clinic, Rochester, Minnesota.

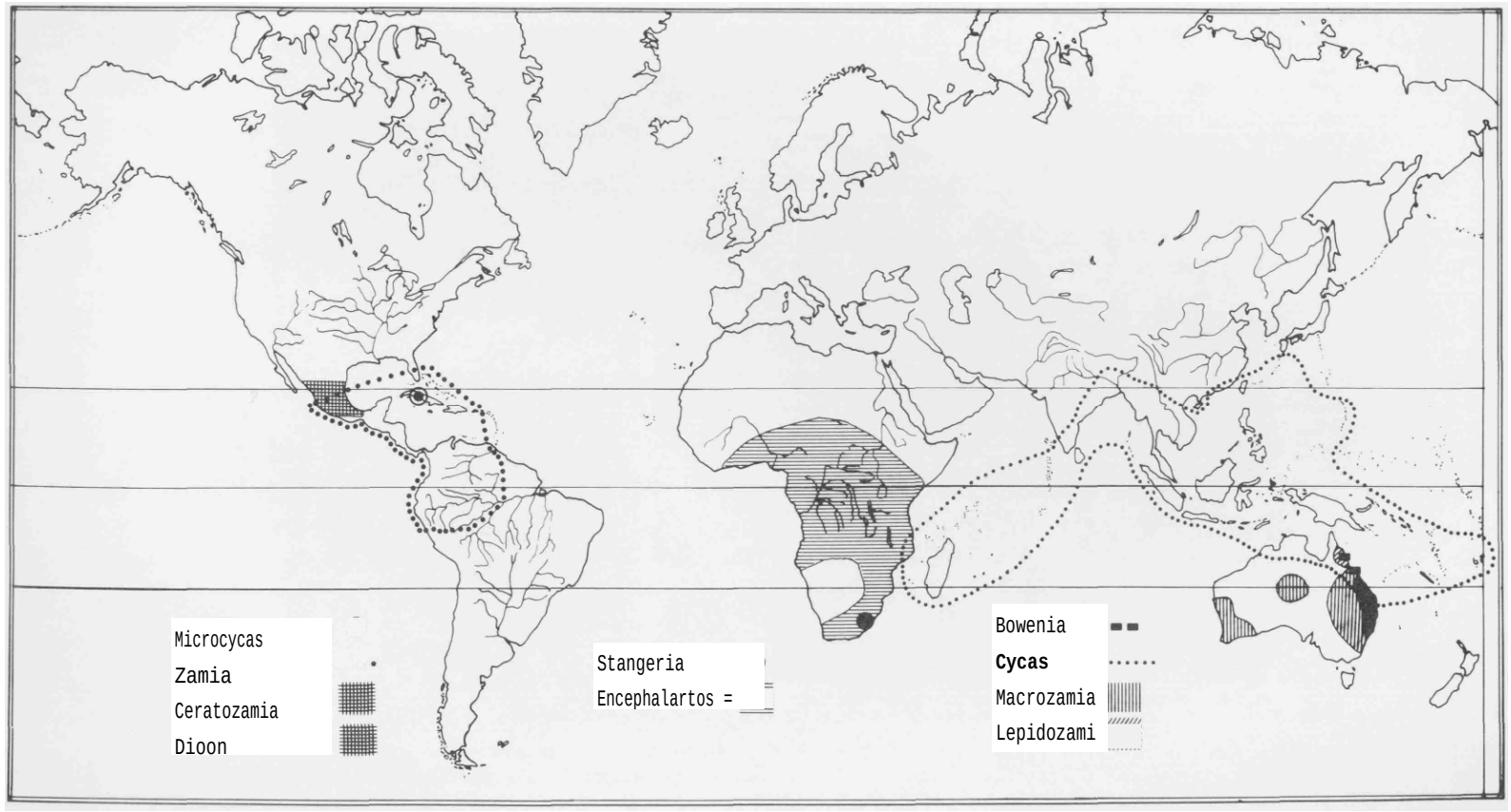
one. A young woman "knew" she had lytiko when she dropped her baby. She was walking home from the fields carrying her baby in her arms. It started to rain, and she started to run and dropped the child. Then she knew she had lytiko!

One of the first popular stories I heard about the high incidence of ALS in Guam was the well-known tale about the priest's mango tree near the church; a large number of people in Umatac were named Quinata (a common name and an extended family in the heavily ALS-afflicted village), and many had ALS. The priest was reputed to have put a curse on those who stole his mangoes and perhaps on the Quinata family.

When I returned to the United States, my first stop in Cambridge was at the botanical library. In Australia, I read, where large herds of cattle were being introduced, the cattle soon found a favorite food—the new green shoots of cycads—and would walk some distance to find them. But after about two weeks on this diet, they were afflicted with a hind-leg paralysis known locally as "rickets" or "wobbles." Soon they were unable to walk and, unless hand-fed, died of starvation. Losses were heavy. Similar reports came from other areas where cycads grew. Controlled experiments confirmed the field observations. This work continued but no specific neurotoxic agent was identified (see Altenkirk 1974, Hall 1954, 1987, Hooper 1974, 1978, Innes 1965, Mason 1965) until, after 30 years of intermitent research, a motor-system disease was experimentally produced in monkeys fed a compound from cycads (Spencer 1986, 1987).



Chamorro women making cycad tortillas.



Map showing distribution of cycads.

CYCADALES (Johnson 1959)

Cycads presently are regarded as primitive "gymnosperms" and are treated in botanical classification as Order Cycadales in the Class Cyca-dapsida.
Cycadaceae L. C. Rich. *In* Persoon, Synopsis Plantarum, seu Enchiridium Botanicum 2:630-631. 1807.

1. *Cycas L.* Stangeriaceae L. A. S. Johnson 1959.
2. *Stangeria T.* Moore Zamiaceae Reichenbach 1837.

TRIBE Encephalarteae (Miquel) L. A. S. Johnson 1959.

3. *Lepidozamia* Regel
4. *Macrozamia* Miquel Sect. Macrozamia Sect. Parazamia
5. *Encephalartos* Lehmann TRIBE Dioneae (Schuster) L. A. S. Johnson 1959.
6. *Dioon* Lindley

TRIBE Zamieae.

7. *Microcycas* (Miquel) De Candolle
8. *Ceratozamia* Brongniart
9. *Zamia L.* 10. *Bowenia* Hooker ex Hooker f.

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1829-1989

Freycinet, Louis C. D. de

1829. Voyage autour du monde, entrepris par ordre du roi. Execute sur les corvettes de S. M. l'Uranie et la Physicienne, pendant les annees l817, 1818, 1819, et 1820. Vol. 1, part 2./ Imprimeria Royale, Paris. (Unpublished translation from French by Erica Steele, Honolulu, HI)

Although cycads were indigenous to the islands, they were not a part of the Mariana Islands diet until the people were shown how to extract the flour from the pith of the stem and from the pit (endosperm) of the seeds. By 1819 the cultivation of cycads ranked first in the agricultural industry on Guam.

The Chamorros first learned to process and detoxify the seed and stem of the cycad from the Spanish. Processing included soaking for ten days, drying in the sun, and grinding on a stone metate. Popular dishes were "atole" and "tortillas."

This book includes a description of the death of half the crew of the *M. Quoy* because of the consumption of poorly prepared cycad flour.

Villalobos, Francisco Ramon

1833. Geographic, military and political description of the island of Guam. Unpubl. manuscript, Micronesian Area Center, Univ. Guam, Agana, Guam. (English transl. by Sr. Felicia Plaza, 1969.)

P. 58 of manuscript (pp. 35-36 of translation): "The countryside is plentiful in wild hogs, deer, coconut trees, bread-fruit trees, and dugdug *(Artocarpus communis).* The two latter provide for the equivalent of bread. Flour and bread can be made from a palm called federico, which abounds on the island. The federico *(Cycas circinalis)* is a palm-like tree, with an erect, scaley trunk bearing no branches or leaves but three rods* from the ground, it bears a crown of glossy, fern-like, stiff, thick leaves, bearing nuts which in their crude state are poisonous, but become edible after macerated in water and exposed to the sun. A very white and palatable flour similar to that extracted from the federico, is also made from the tuberous root called gangan."

*1 rod= 16.5ft.

Jackson, J. R.
1864. Cycads/Intellectual Observ. 5:246-252.

Excellent, general review (p. 251). Gum from *Cycas circinalis* is reputed to be a good antidote for snake bites and is also used for ulcers of all descriptions in India, Fiji, and Ceylon (p. 252). In the Bahamas, starch is obtained from the trunk of *Encephalartos tensus* Willd.

Ibanez del Carmen, Aniceto, Curo parroco de Agana
1865. Diccionario Espanol-Chamorro/Imp. de Ramirez y Giraudier, Manila.

P. 61: nuez (nux) vomica s. f.* fadang

Earliest dictionary reference found for fadang (cycad starch).

Drury, H.
1873. The useful plants of India/William H. Alien and Co., London. Pp. 171-172.

From text p. 171: "MEDICAL USES.—The scales of the cone are a most useful narcotic medicine, and are commonly sold in the bazaars. A gummy substance which exudes from the stem produces rapid suppuration in malignant ulcers. The fruit bearing cone reduced to poultice is applied to the loins for the removal of nephritic pains.

Pp. 171-172: "ECONOMIC USES.—This is a singular-looking plant, very abundant in the forests of Malabar and Cochin. It is very fertile, and easily propagated both from nuts and branches. Its vitality is said to be remarkable, insomuch that the tree, having been taken up and put down again a second time after one or two years, it will grow. A kind of sago is prepared from the nuts. In order to collect it the latter are dried in the sun for about a month, beaten in a mortar, and the kernel made into flour. It is much used by the poorer classes of natives and forest tribes. It, however, will not keep long."

Corte y Ruano Calderon, Felipe Maria de la
1875. Memoria Descriptiva e Historica de las Islas Marianas/Imprenta Nacional, Madrid. 260 p. Translation provided by Micronesian Area Research Center, University of Guam.

From text p. 57: "The federico or fadang is another small palm tree that produces much fruit in the shape of coconuts, but only about two inches, with a white compact marrow or almond which is poisonous, but when soaked either in small pieces or scraped on stones, it undergoes a fermentation and is rinsed several times and then dried, it can be ground to form a kind of bread or somewhat glutinous cake, although not an unpleasant

*s. f. = sans fuertes (without date)

food which the natives use quite a lot of. This palm tree is rarely found ten feet high and generally does not reach six.

"It grows quite abundantly in stony places. Gluten is made from its flour used as starch, although it is not very white and gives off rather an unpleasant smell. It would perhaps be preferable for other similar uses, than any other class, taking it without fermenting, because it seems insects attack it with difficulty. It is said in the country that continuous use of this food produces tenesmus, which proves that in spite of the treatment it undergoes, it is not completely cured. On a good diet it seems this food should not be included as it is so easy to obtain other better ones but in Guam the best is what is found without prevision, and calculated work, although actually picking and preparing it takes longer than a similar amount of maize or other better foods. But maize needs working with a five month interval and the federico comes directly after it is found without having planted or even thought about it."

Maiden, J. H.

1889. The Useful Native Plants of Australia/Technol. Mus. New South Wales, Sydney, Aust. P. 218.

Annotation: *Macrozamia peroffskyana:* "A small quantity of gum of this species has been received at the Technological Museum. It is in flattened pieces, reminding one strongly of 'button lac,' but much lighter in colour even than the 'fine button lac' of commerce. The flattened shape is due to the mode of collecting it. A spontaneous flow of gum does not appear to occur in any species, but from the cut ends of the cones and bases of leaves it exudes more or less freely. If put to drain on a plate, the flattened shapes of 'button lac' will be very readily obtained. If one of these flattened pieces be placed in water, it begins to swell immediately, and this absorption of water goes on for several days, by the end of which period it has swelled to about fifty times its original size. It then presents the appearance of an almost colourless, quivering jelly. This jelly assumes a pseudo-crystalline appearance, forming angular masses. This result is, of course, in consequence of the minute fissures in the dried gum. It breaks readily, has a bright fracture, and in the mouth feels somewhat like tragacanth."

Turner, F.

1893. The zamia palm *(Macrozamia miquelii* F.v.M.) and its relation to the disease known as rickets in cattle/Agr. Gaz. New South Wales 4:158-161.

Turner fed a heifer scorched zamia plants along with a nutritious diet. On the 14th day the symptoms of rickets were well developed. Aborigines were well aware of the poisonous prop-

erties. To prepare for eating, they pounded the kernels and put them in a dilly bag, which they placed in a stream or water hole for about six days. The mass was baked in ashes, similar to the way that damper is cooked by white people.

Edwards, H. H.
1894. Report on the disease known as "rickets" or "wobbles"/J. Bur. Agr. W. Aust. 1 (18): 225-234 (Nov. 27).

Known at least since 1865 in Western Australia. A detailed description of signs and progress of the ailment in cattle. Illustrated.

Lamb, S.
1895. Plants injurious to stock/Agr. Gaz. New South Wales 6:505.

"When I was in North Queensland many cattle were dying of paralysis of the hind quarters. Mr. W. Brown, of Zeppen, near Rockhampton, who lost many, attributed the disease to the cattle eating the shoots of the Zamia.

"When at Denman last week I found *Zamia* growing in great profusion on the ridges. Many of the plants had evidently been browsed. I therefore made inquiry as to any deaths or sickness among cattle there. Mr. Doyle, who has resided very many years in the district, said he well knew the complaint from my description, but he had never seen or heard of a case occurring amongst the stock grazing on those ridges.

"Whether the *Zamia* growing on the ridges above Denman is identical with that growing on the low country between Rockhampton and Byfield, I am not in a position to say but they certainly have a strong resemblance to each other; further, if they are the same, it is possible that those growing on dry ridges may not be so hurtful as those growing in swampy country."

Bailey, F. M.
1897. Plants reputed poisonous and injurious to stock/Queensland Agr. J. 2 (2): 3-4.

Family Cycadaceae: *Macrozamia miquelii* is considered to produce "rickets" in cattle, and other species are suspected. Distinguishing symptoms are described. To eliminate cycads from pastures, Bailey proposes that "fruits" (seeds) of all cycad plants should be carefully destroyed before they come to maturity.

Carson, J.
1898. Arrowroot, cassava and koonti/Amer. J. Pharm. 70:212-214.

Key West market. Used by "poor whites" in Florida and by soldiers. Pipe bowls were made from dried root. There were numerous starch factories in south Florida. Many considered cycad starch the "best" Bermuda starch. Process: a hollow (9

in. x 9 in.) cut in a large pine trunk was used as a mortar with a hardwood pestle. *Zamia integrifolia* root was chopped with water in a bark vessel, mashed in a cloth, and strained into a deerhide vessel (called "tuckahoe" by Seminóles and soldiers.)

Coe, C. H.

1898. The koontee, the Seminóle bread root/Sci. Amer. Supp. 1181. Aug. 20.

"Koontee or koonti—*Zamia integrifolia.* Sometimes the half-wild hogs succeed in partially uprooting the plant. A fine quality of starch or flour is made from the root . . . fully equal to the best Jamaica and Bermuda arrowroot. Among the Seminóles it takes the place of wheat. White residents used it in place of corn starch. Preparation (Indian method): roots washed, chopped into small pieces and pounded to a pulp in a mortar or trough cut for this purpose in a log. Mass then removed and placed in a tub of water where it is allowed to thoroughly macerate, after which it is strained through a coarse cloth. The starch is caught in a tub or deerhide while the useless fiber is discarded. When the starch has settled, the water is carefully drained away and the dried whitish residue is spread on a flat surface such as a deerhide. This method is improved by the whites who generally grate or grind the roots, and repeatedly saturate and dry the product to a beautiful white color. Principal use is for bread for the Seminóles characterized by an orange or yellowish white tinge and insipid taste due to lack of salt. For the Indians—it is the staff of life—always available, ready for gathering at any season. Large quantities were found and destroyed by our troops while scouting the Everglades."

Amount estimated: In 1845 a committee of the Territorial Legislature of Florida reported that "at least 25,000 lbs of prepared koontee had been made during that year for shipment presumably to foreign markets via Key West. In 1843 a koontee mill was erected on Biscayne Bay. An earlier authority also refers to large European shipments.

[Ref. (1) Senate report 242, 1st Sess. 30th U.S. Congress, 1845. (2) St. Augustine News, Dec. 30, 1843. (3) Roman's History of Florida, 1775.]

Crawley, A. W. V.

1898. Producers' Gazette of Settlers' Record/W. Aust. 5 (1): 399-403.

Crawley describes the afflicted bullocks at Harvey: First, a wobbly gait, with great difficulty in walking downhill, with gradual loss of use of the hind quarters, the cattle eventually falling and being unable to rise. A peculiar curve of the spine in front of the loins now becomes visible, gradually becoming

worse. The animal, which at first lies well up on its sternum, gradually seems to lose the power of supporting itself as before and lies down flat on the side with the head sometimes stretched out, and at others, drawn back. The eyes are bright and sometimes protrude slightly; later they are dull and shrunken. The bowels are very constipated, the feces sometimes showing mucous and even blood. Urination is sometimes frequent and involuntary, sometimes normal and, in one case, stoppage occurred. The hindlegs are cold, weak, trembling, and extended backwards. The appetite is poor. The animal gradually grows weaker. Trismus is sometimes present. Finally the animal dies after lying four-ten days in a hopeless semiparalyzed condition.

A postmortem examination shows the remains of *Zamia* (cycad) in the stomach. The omasum and abomasum are dry. There is some congestion of the organs. The spinal cord and membranes are injected and meninges thickened and the arachnoid covered with an exúdate, which sometimes joins its opposed surfaces, and sometimes consists of a semipurulent fluid. The spinal cord is considerably softened, sometimes only in the lumbar region, sometimes nearly along its whole length. Sometimes the spinal cord and meninges are highly congested.

Maiden, J. H.

1899a. Native food plants/Agr. Gaz. New South Wales 10 (Pt. 4): 730-740.

Maiden states that the nuts of *Macrozamia* caused poisoning of three boys at Springsure, Queensland. The plant was tested by the Poison Plants Committee in New South Wales and the seeds were found to be poisonous for cattle and sheep. The kernels were toxic and the red rind (testa) led to symptoms of enteritis followed by recovery. (N.S.W. Dept. Agr. Rec.) (See also Hurst 1942.)

Maiden, J. H.

1899b. Effects on cattle of eating *Macrozamia* roots/Agr. Gaz. New South Wales 10 (12): 1259 (Dec.)

"Burrawangs" or "blackfellow's potatoes" are common names for the seeds of *Macrozamia,* which are considered the cause of "rickets" (paralysis) in stock. It is observed that after cattle get into the habit of eating this plant they have a craving for it even when the leaves and roots have been lying on the ground for three years or so.

Stewart, J. D.

1899. A report on the disease affecting cattle in the Moruya District/ Agr. Gaz. New South Wales 10 (11): 1205-1210.

The disease, which is known locally as "rickets" or "ricketty," was first noticed about July 1898 when it affected a few head of

cattle belonging to one owner. Since then it has become more prevalent. About 100 head of cattle, belonging to several owners and occupying different paddocks, have manifested signs. The disease affects cattle of all sexes from 6 months old upwards. It is prevalent among yearlings. (There follows a detailed description of signs and postmortem appearances. Specimens were collected and sent to the Health Dept. Photographs show stages of the disease.) Roth, W. E.

1901. Food: its search, capture and preparation/N. Queensland Ethnogr. Bull. 3:114-115. G. A. Vaughane, publisher.

From text: *Cycas media*, R. Br. "Zamia." "On the Bloomfield River, 'fruits' (seeds) are fit to eat from July to January. The seeds are gathered by old men, women, and girls. They are roasted and cracked, the kernels being kept for some four or five days before being pounded up into flour by the women. The reason for letting these few days elapse is said to be that the delay helps to make them pound up more finely. The pounded seed is next sifted through a palm-fiber dilly bag, which, having a mesh with smaller interspaces than the other varieties of bag, prevents the coarser particles (from) getting through. The flour is next put into a grass dilly bag, which has been previously folded sideways upon itself so as to form a basin-like receptacle, and placed near a stream. With the help of leaves acting as a trough, water is allowed to continue flowing into the receptacle, matters being so regulated that the water never overflows the edges. Fresh water is thus continuously percolating through the *Zamia* flour in its dilly bag colander throughout the night, and in the morning it is ready to be eaten. It may be kept for some three or four days, however, up to which time it is believed to improve; it will not keep any longer than that (R. Hislop). On the lower Tully River what is steamed and cut up and rushing water is made to fall from a height on to the contents of the dilly bag held below so as to keep the mass both strained and well stirred—a process that is kept up continuously for quite a day."

P. 14a, *Macrozamia miquelii*, F. v. M. "The seeds . . . are baked for about half an hour under ashes; the outside covers and the stones (pits) are then broken, and the kernels, divided by a stroke of the 'kondola' (pounding-stone), are put into a dilly bag and carried to a stream or pond, where they remain six or eight days before they are fit for eating." (A. Thozet).

Van Dongen, J.

1903. *Cycas circinalis* L./Pharm. Weekbl. Nederland 40:309-313. (Transl. for the Natl. Inst. of Neurol. Dis. and Blind., Epidemiol. Branch.)

From Dr. Tilley: large areas of Zamia country were either abandoned or cleared of *Zamia.* With removal, the disease has disappeared. In cattle, the disease was formerly known as "rickets."

Ewart, A. J. & J. R. Tovey
1909. The Weeds, Poison Plants, and Naturalized Aliens of Victoria/ J. Kemp, Govt. Printer, Min. Agr., Melbourne, Australia.

P. 110: "In New South Wales and Queensland several species of *Macrozamia,* and also *Cycas media,* R. Br., are supposed to produce partial muscular paralysis in stock, which has become fond of eating them. A poisonous resin has been extracted and this produced fatal gastro-enteritis when given internally to guinea pigs and cats. Animals fed with the plant showed similar symptoms. When small quantities are continually eaten, the usual chronic effects gradually ensue, which are grouped together under the head of 'wobbles' disease. It is possible or may be due in part at least, to the indigestible character of the food swallowed."

Gifford, J.
1912. The Everglades and Other Essays Relating to Southern Florida/ 2nd ed. Everglade Land Sales Co., Miami. 222 pp.

P. 100: "Grown in Andros Is. in the Bahamas, sold in Nassau (vern: bay rush). Fires sweep, but koonti is safe since the main part of plant is underground. . . . Animals which drink the red water from washing the starch usually die, not a quick death but a slow poisoning. . . . Natives say crows eat comptie corn (seeds like large grains of fresh corn) and live, but turkeys kill themselves by eating koonti corn." p. 175: "Koonti is only root crop capable of capturing its own nitrogen from the air or the soil by means of large bacterial nodules or roots. High-dry land is never flooded where 'koonti' grows."

Marks, G.
1912. *Zamia* country in Tabulam district/Agrie. Gaz. New South Wales 23 (12): 1056-1058. (From Hurst 1942.)

Describes an investigation of an outbreak in Tabulam district, New South Wales, where more than 400 head of cattle died. Some years later, cattle were again affected on the same range. This poisoning was reputedly due to the consumption of *Macrozamia.* Losses became so heavy each year that the leases were finally given up and the country affected by "zamia" poisoning was cut off. Some years later, the land was again leased for grazing, but the cattle were affected as before with many fatalities occurring. Described as a condition of partial paralysis and loosening of the horns, sometimes death.

Clevenger, J. F.
1913. A report on the Zamia starch situation/ J. Amer. Pharm. Assoc. 10:837-840.

Juritz, C. F.
1914. South African plant poisons and their investigation/S. African J. Sci. 11:109.

Re: *Encephalartos* spp. Dr. Rattray claims to eat ripe seed of cycads without ill effect. Gum from the plant is also eaten. Africans in E. London area generally regard seeds as edible. Monkeys eat flesh but discard kernel. Pulp not unpleasant but kernel astringent like acorn. Two Zulu boys are reported to have died from eating the seeds.

Anon.
1916. Guam Agr. Exp. Stn. Rep. U.S. Govt. Printing Off., Washington.

P. 42: *"Cycas.* This plant has a very beautiful palmlike trunk crowned with stiff fernlike leaves and bearing seeds called federico [Spanish origin] or fadang [Chamorro language]. The plant grows wild throughout the island especially in rough, rocky places. The seeds are poisonous until they have been soaked for several hours in successive changes of water. Starch made from the seeds is used as a food by a great many of the natives. It is of a high quality but has a disagreeable odor.

"The cycads have played an important part in the life of the people of the island. Hurricanes or typhoons have at times destroyed large quantities of food, after which the people have gathered federico seeds and lived largely on them until other food became available."

Chamberlain, C. J.
1919. The Living Cycads/Chicago 172 pp. (Facsimile 1965 edition.)

This field study extended over more than 15 years prior to 1919. Nine genera and many of the species are included. Part I includes the distribution, general appearance, and field conditions of the cycads. Part II presents the life history of the group based upon the author's own observations. Part III is devoted to the evolution and the phylogeny of the cycads.

Pétrie, J. M.
1920. The chemical examination of *Macrozamia spiralis/Linn.* Soc. New South Wales 45, Pt. 3 (179): 424-442.

Pétrie provides an excellent historical report of the research on *Macrozamia spiralis* prior to 1920.

Standley, P. C.
1920. Trees and shrubs of Mexico/Contr. U. S. Nati. Herb. 23 (1): 47-50.

Dioon edule L.: "The large chestnut-like seeds contain much starch, and are roasted or boiled and eaten. They are a favorite food of bears, peccaries, and domestic swine. A decoction of the seeds is said to be used for neuralgia. The staminate inflorescences are claimed to be poisonous to cattle, causing emaciation and partial paralysis. The plant is often seen in cultivation."

Baldwin, W.

1921. Seminóle bread—the Conti/J. N. Y. Bot. Gard. 22:121-137 (June 26).

Records of Hernando de Escalante Fontanda in 16th century indicate Indians of Florida made white bread of Zamia root. Flour called "kunti hatki" (white) and "kunti tsohati" (red); ("kunti" or "coontia").

Clark, A. M.

1922-27. Diseases of farm animals and their treatment/W. Aust. Dept. Agr., Leafl. 187, Govt. Printer, Perth, Aust. 26 pp.

P. 16, *Zamia* palm poisoning: "... common in dairy cattle which have been running out in the bush in the south-west portion of the state. It is due to the cattle eating the palm and nut, which contains a poison that acts on the nervous system, producing permanent changes in the spinal cord—hence, the partial loss of power in the hind legs. . . ."

Treatment: Salts, salt, ginger, molasses, "but not much use."

Basedow, H. H.

1925. The Australian Aboriginal/F. W. Reece and Sons, Adelaide, Aust.

P. 77: Handball was played with *Macrozamia* nuts; two examples are on this page, one from Bathhurst I. and the other from Armhem land.

Britton, N. L. & P. Wilson

1926. Cycad paralysis in cattle in Puerto Rico. Cycadaceae/Scientific survey of Puerto Rico and the Virgin Islands. N.Y. Acad. Sci. 6 (3): 329-330.

This plant *(Zamia portoricensis* Urban) is reported by residents of a region in southwest P.R. (where it grows) to cause a paralysis known as "ranilla" in cattle that eat the leaves.

Seddon, H. R.

1930. A review of plants poisonous to livestock/Agr. Gaz. New South Wales 41 (9): 637-644 (Sept.).

Ochse, J. J. & R. C. Bakhuizen Van Den Brink

1931. Vegetables of the Dutch East Indies/Dept. Agr., Indust. & Comm. Netherland East Indies, Buitenzorg, Java. Pp. 215-217.

Precaution re. the preparation of cycad seeds: "One should not eat the fruits if one does not know how to prepare them"—a long and complicated process. In the Moluccas, one hears that eating much sayor kalapa, from *Cycas rhumphii* Miq., causes rheumatism.

Nishida, K.

1934. Sago palm *(Cycas revoluta)* starch and sago palm miso (paste), special products in Oshima region in Kagoshima Prefecture/ Nippon Jozokyokai Zasshi 12 (4): 271-278. (In Japanese with English summary.)

From English summary: "I examined the actual uses of the sago palm in Oshima. . . . In addition to the wide use of its starch for other food, it is used as the material for miso, as medicine, as fertilizer and for decoration and appreciation. For its medicinal and appreciation purposes, it is shipped to Japan proper, and for decoration uses, the leaves are exported to Europe and America."

This extensive journal article provides details of the care and preparation of many cycad preparations commonly used in these islands and on the nearby mainland. The process of fermentation is described in detail.

Burkill, I. H.

1935. A Dictionary of the Economic Products of the Malay Peninsula/London. Vol. 1: Pp. 718-721.

For the countries in the Malay Peninsula, use of cycads for food and medicine are similar to those in Southeast Asia today.

Nishida, K.

1936a. Fermentation in seeds of *Cycas revoluta*/J. Soc. Fermentation Tech. 14:302-313.

By soaking seeds for 5 h or by steaming material, HCHO was eliminated and they were no longer toxic to small birds. This demonstrated that *C. revoluta* can be used as a substitute for rice, wheat, and miso or for making soy sauce.

Nishida, K.

1936b. Preparation of cycad-food by removal of the toxic components from cycad nuts/J. Soc. Fermentation Tech. 14 (10): 823-833. (In Japanese with English transa.)

In this brief report of preparation of starch from cycad nuts, no mention is made of a fermentation procedure. Safety in eating the product seems to be assured by the reduction of formaldehyde content. The reference is short and has no further information.

Nishida, K.
1936c. Biochemical studies of "sotetsu" *(Cycas revoluta* Thunb.). Poison removal and nutritional value of "sotetsu" seeds/Nippon Nogeikagaku Kaishi (J. Agr. Chem. Soc. Japan) 12 (11): 1106-1116. (In Japanese with English transa.)

Nishida found that "poison" was not completely removed from cycad starch after extensive soaking. However, safety was somewhat improved for seed starch when it was steamed for 90 min. Testing was done with small birds *(Uroloncha domestica),* quail, white mice, and white rats. Nishida believed the toxic component was formaldehyde.

Cooper, J. M.
1941. Isolation of a toxic principle from the seeds of *Macrozamia spiralis/3.* Proc. Roy. Soc. New South Wales 74 (4): 450-454.

From summary: Describes "... the isolation of a crystalline substance from the seeds of *Macrozamia spiralis.* It is toxic to guinea-pigs when administered orally, but not when injected subcutaneously."

Roberts, G. A.
1941. Paraplegia (wobbles) in cattle/Vet. Med. 36 (1): 507-509. (Oct.)

"The cause of Zamia paralysis lies in continued consumption of Zamia leaves."

Thompson, L.
1941. Guam and Its People: A Study of Culture Change and Colonial Education. #8/Amer. Council, Inst. Pac. Rel, New York, 367 pp.

An excellent study of the people of Guam. Two references to the use of cycad as food. (See p. 18 "federico palm" and p. 92 "federico fruit," famine food.)

Hurst, E.
1942. Poison plants of New South Wales/New South Wales Poison Plants Comm., Univ. Sydney, and New South Wales Dept. Agr. 498 pp.

A well-documented review of toxic plants of the area, with an especially good section on cycads and their toxic effects on cattle.

Alien, P. H.
1943. Poisonous and Injurious Plants of Panama/Williams and Wilkins Co., Baltimore.

P. 31: "Particularly infamous is *Zamia furfuraceae* L., native to Honduras, where the plants have been used for criminal poisonings, and for the destruction of noxious animals."

Merrill, E. D.
1943. Emergency Food Plants & Poisonous Plants of the Islands of the Pacific/Tech. Manual 10-420. War Dept., Wash., D.C. Pp. 116-119.

Includes tabulation, notes, and sketches of edible poisonous Pacific plants.

Gifford, J. C.
1945. Five Native Florida Plants. Living by the Land/Glade House, Coral Gables. 139pp.

The underground portion of the cycad, one of these plants, is a good source of starch. The stem is pounded to a pulp and washed in a straining cloth to remove the poison. The plant does not grow fast enough to have much commercial value. The seeds from the cones resemble corn and are called "koontie corn," "comptie," or "koonti."

Harvey, A.
1945. Food preservation in Australian tribes/Mankind 3 (7) : 191 -192.

Purpose of preservation: future feasts and future shortages. Husk: edible raw. Kernel: must be soaked in water to remove caustic properties or can be cooked in hot ashes and eaten directly. Preservation: nut cut into slices, husk and pith together, dried in the sun for two or three days, then rolled in cylinders of paper bark. It will keep thus for months. The ripening process counteracts the caustic properties of the kernel, which may be eaten cooked or raw.

Large trenches are dug about 20 ft. long, 2 ft. wide, and 1 ft. deep and lined with grass. The nuts are broken open out of the shell into the trench in layers and covered with earth. The nuts ripen naturally, and after two or three months they are dug up and pulverized on grinding stones. This powder is moistened with saliva and made into large, flat slabs and cooked in hot ashes. With a paper-bark cover, they are readily transported and are articles of trade and ceremony. The tribes of this area have an "increase center" for the cycad at Manangura, some seven miles from the mouth of the MacArthur River.

Gifford, J. C.
1946. Some reflections on the South Florida of long ago/J. Hist. Assoc. S. Florida. Pp. 38-43.

Homesteaders settled in South Florida and set up "comptie" mills for the extraction of starch from cycads. Barrels of snow-white starch were shipped by sailboat to Key West and then elsewhere by steamer.

Preparation: Indians hollowed out pine logs in the shape of troughs. After washing off the dirt, the women pounded roots

into pulp with a heavy wooden pestle. They filled the troughs with water. The floating roughage was thrown out and the white farina settled to the bottom. After it was thoroughly washed and dried in the sun, it furnished an essential food for the "whites," "blacks," and "reds." The red wash water from the washings was poisonous and if a dog or other animal drank from the puddle, he soon died a painful death. This industry ended with the exhaustion of the "comptie."

Ricourt y Regus, R. S.

1947. Contribución al estudio de las Zamias en la República Dominicana/Anales Univ. Santo Domingo 12 (41-44): 171-180 (Jan.-Dec). (Transl. from Spanish at Natl. Inst. Health.)

It is said the seeds of *Cycas circinalis* are used as a narcotic; from the stem a gummy substance is used for treating ulcers. Extraction of the starch is a small family industry. It is used for sizing when ironing in place of yucca starch. It is also used as a food: biscuits, certain rolls called "cholas," and other specialties called "hojaldres" or "tortillitas."

Some cattle that graze where Zamia grows develop a paralysis commonly called "derriengue." The specific cause is not understood.

All *Zamia* that grows in the Dominican Republic is known as "guayiga."

Steyne, D. G., S. J. Van der Walt & I. C. Verdoorn

1948. The seeds of some species of *Encephalartos* (cycads). A report on their toxicity/S. African Med. J. 5 (22): 758-760 (Dec.).

The outer fleshy coverings of the fruit were not toxic to rabbits but may contain enough of the toxic principle to poison man. Monkeys and baboons eat the outer fleshy part but discard the "stone." The kernel contains a virulent poison. Symptoms and postmortem findings are described.

Williams, P. O.

1949. The Useful and Ornamental Plants in *Zanzibar* and Pemba/*Zanzibar* Protectorate, Govt. Printer, *Zanzibar*.

P. 222: In Pemba the large fruits, picked when fully ripe, are split and the flesh removed and dried in the sun for about four days, when it becomes as hard as a stone. It is then fermented for a week in a "debe" (tin) with layers of banana leaves, after which it is cleaned of mold, soaked in water to soften for a future day, and then powdered to a flour and used as porridge. Sometimes, after more prolonged storage with the banana leaves, the flesh is boiled and dressed with coconut juice as a vegetable. The starchy mass in the core of the trunk is called "mgwede." It is chopped into small pieces, then heaped for

about a week to allow it to ferment for "neutralizing certain toxic substances." The pieces are then washed, preferably in hot water, and dried in the sun. They are then pounded to a powder and cooked as needed into a porridge known as "ugali."

Heyne, K.
1950. De Nuttige Planten von Indonesie/3rd ed. 's-Gravenhage, van Hoeve. Vol. 1:106-108.

Hertrich, W.
1951. Palms and Cycads, Their Culture in Southern California/Huntington Libr., San Marino. 141 pp.

Quisumbing, E.
1951. Medicinal Plants of the Philippines. Tech. Bull. Dept. Agr. Philipp. Isl. 16: Cycadaceae. Bureau of Printing, Manila. 1234pp.

A compendium of uses reported from many tropical countries.

P. 73-76: Cycad fruit is used as an expectorant and tonic; powder is applied to wounds. Seeds are used as a staple in times of scarcity. Seeds are also eaten in India, Andaman, the Malay Peninsula, and the Dutch East Indies. In some parts of the Philippines the young leaves (still rolled up) are cooked and eaten as a vegetable.

Haring, D. G.
1952. The Island of *Amami Oshima* in the Northern Ryukyus. Pac. Sci. Bd., Natl. Res. Council. *Scientific Investigations in the Ryukyu Islands (SIRI).* Mimeograph, 86 pp. and map. Wash., D.C. U.S. Army Contr. 49-083. OSA 255.

"The foregoing menus fail to indicate the large reliance upon ground cycad *(sotetsu)* nuts on Amami Oshima. Amamians themselves refer to their island as "The Cycad Hell"—a nickname also applied derisively by outsiders. The cycad is a less useful relative of the sago palm. It grows very well in Amami's poorer soils, on steep hillsides—anywhere, in fact, for a variety of factors conspire to make Amami ideal for cycads. Moreover, droughts, floods, and typhoons seem to have little effect on the ubiquitous cycads. Economically the cycad has been a real asset only in prewar years, when the long, durable green fronds were exported in quantities to Java for use as funeral decorations. Its value to Amamians, now that the Java market has vanished, is as a backlog when other crops fail through drought or storm damage—occurrences all too frequent. So the large orange nuts that grow in a cluster atop the stems of cycads are harvested, shelled, dried, and ground to a sort of meal as a reserve against emergencies. Cycad meal is prepared variously, mixed with other foods to stretch them out, made into *sake*—and universally disliked. In addition, as noted previously, it is slightly poi-

sonous and every now and then a batch of especial potency kills those who eat or drink the product. In famine or near-famine, however, any food counts and aversions are discounted in favor of survival. In slavery days cycads had to enter more largely into the diet than now, since nearly all land was used to grow sugar for export.

"In connection with cycads, another menace looms large. The poisonous *habu* vipers often nest atop cycads and lay their eggs among the nuts. When a peasant reaches up to gather the nuts, the snake strikes, and one more death swells the total. This adds one more reason why the cycad is disliked even though it provides emergency food and liquor. It is apparent that the good housewife who listed her menus said nothing about dishes containing cycad; she serves them only *in extremis*, although she probably keeps the meal on hand."

Note: During a more recent visit to Amami Oshima, it was observed that cycad meal was being added as an extender to miso and eaten by some families three or four times a day after the mixture was fermented. A large market was reported for this product in Japan as well as on Amami—Ed.

Smith, A. H.

1952. 40R. Mimeograph. U.S. Army Contr. 49-083, OSA 255.

P 18: Smith, an anthropologist in Yaeyama for SIRI, reports that in Yaeyama, cycad seeds are removed from their deep orange shells, returned to their leaf-covered baskets, put outside, and allowed to mold. When completely covered with mold, they are thoroughly washed in a flowing stream and then pulverized into flour for winter use.

Hall, W. T. K.

1954. Zamia staggers in cattle/Queensland Agr. J. 79:173-177.

Chronic condition appears within a few weeks.

Razafimahery, R.

1954. Glucosides cyanogenetiques pois du cap, manioc et "bononoka" *(Cycas thouarsii)/B\ù*. Acad. Malgache. 31:71-77. (In French.)

Riggs, N. V.

1954. The occurrence of macrozamin in the seeds of cycads. Aust. J. Chem. 7(1): 123-124.

Macrozamin "I" was isolated through its hexacetate from the methanolic extract of the seeds of *Cycas media, Bowenia serrata,* and *Macrozamia miquelii.* The presence of "I" was indicated also in *M. moorei, M. paulo-gulielmi, M. douglasi, M. hopei,* and *B. spectabilis* by aqueous extract of their seeds, whereas *M. denisoni* gave negative results in the same tests.

Kobayashi, A.
1955. Uses of the sago palm, *Cycas revoluta* Thunb. in Amami Oshima/Unpubl. rep., Univ. Kagoshima, pp. 15-19. (Transl, from Japanese by Keiko Hirano, Oct. 1955.)

" 1. This is the process which I actually observed: After removal of the outer scaly skin, the stem was cut into small pieces, 7-15 cm., and then left for some time under a straw mat so that it might become covered with fungi. The stem pieces fermented by the effect of the black fungi and others. Isolation of the starch was now easier and the toxic elements were removed. They were washed in water and then the starch was extracted using the ordinary method.
"2. The leaves are rich in nitrogen and used as green fertilizer for rice and sugar-cane. The leaves are also used and sold for decoration. "3. The seed is used as material for miso or bean paste."

Fosberg, F. R.
1956. Letter to M. G. Whiting, Aug. 16, 1956, Miyako Island, Ryukyus.

Included are the following comments: Many persons aged 18-20 were reported to be dying of "old age." In Ishigaki, he heard of persons dying from eating improperly prepared cycad starch. The head of the health department, a practical medical man, described his own experience after eating improperly prepared starch: heavy perspiration, vomiting, and finally, loss of consciousness. The poisonous principal is thought to be HCN. Preparation: cut seed in half, dry in sun, grate, and wash out the starch. Then wash with constantly changing water.

The "doctor" knew what was meant by "ALS" and said the Japanese name is "kinisyukusei-sokusdu"* and that it was known in Taiwan 20 years ago. He had heard of no cases in the Ryukus but suggested that if there were any, they would be on the island of Kuroshima where more cycad starch is used than in Ishigaki. The seeds are just beginning to ripen on Miyako now.

Gardner, C. A. & H. W. Bennetts
1956. The Toxic Plants of Western Australia/West Australia Newspapers, Ltd., Perth, pp. 5-8.

Macrozamia Reidlei was used for food by natives and early settlers. After drying, the pith of the stem was shredded and soaked in water for about 6 h. It was then shaken up and filtered, the milky fluid being allowed to settle. The sediment was washed several times, dried slowly, and finely powdered. The

*Perhaps also spelled "kinshukusei sokumen kokasho."

natives are said to have buried the seeds or to have baked them before eating. Practically all the species of *Macrozamia* and *Cycas* are considered to cause "rickets" in cattle; the growth on burned land or recently developed land is particularly incriminated. Symptoms and pathology of natural and experimental cases are described.

Footnote: "Sheep were shown by Armstrong, Departmental Record (1955) to be experimentally susceptible to poisoning by the leaves of *M. Reidlei.* One sheep which ate 48 lb. of young leaves in 13 weeks developed a condition similar to zamia 'rickets' in cattle, showing the first signs of affection of the hind limbs at 6 weeks; 10 weeks after the commencement of feeding it was unable to rise and thereafter developed a complete posterior paralysis. It was killed for post-mortem examination. Microscopic examination revealed a demyelination of the spinal cord with a destruction similar to that seen in the case of lambs affected with copper deficiency (enzootic ataxia)."

Hall, W. T. K.

1956. A note on *Macrozamia* poisoning of cattle/Aust. Vet. J. 32:173-175 (July).

Wide variation in amount of plant required to produce symptoms of "rickets." Experimental feeding of leaves to cattle produced symptoms of incoordination and weakness of hindlegs. Green leaves are more toxic than dried leaves; young shoots are more toxic than older leaves. Toxic principle is not labile, and complete recovery does not occur.

Huston, W. J., J. Lingenfelder, D. W. Mulder & L. T. Kurland

1956. Pregnancy complicated by amyotrophic lateral sclerosis/Amer. J. Obst. Gynecol. 72:93-99.

From Summary, p. 99: "The effect of pregnancy on amyotrophic lateral sclerosis and the effect of amyotrophic lateral sclerosis on pregnancy and delivery were studied in 17 patients on the island of Guam. Patients with amyotrophic lateral sclerosis who become pregnant are able, in most instances, to be delivered of normal infants. They frequently need special care, however, because of the problems peculiar to this disease."

P. 96: "Of the 21 children who were born to these 17 women, 19 appeared normal at birth and have remained so to the date of this report. Two of these children had severe congenital anomalies. The mother of one of these infants was 41 years old at the time of the birth of her child, which was an anencephalic monster. The second mother was 37 years old at the birth of their child, who had a cleft palate and harelip."

Riggs, N. V.

1956. Glucosyloxyazoxymethane, a constituent of the seeds of *Cycas circinalis L./Chem.* Ind. 926 (Sept. 8).

A pseudo-cyanogenetic glycoside with the formula C(8)H(16) O(7)N(2) [For the preceding chemical formula, subscripting was not available in this edition.], isolated from seeds of *Cycas circinalis* L. obtained from Guam, Marianas Islands, was found to be similar if not identical to both cycasin and macrozamin, which have been isolated from Japanese, Australian, and African cycads.

Teruya, Hiroyoshi

1956. Cycad poisoning on Miyako. (Adapted from an English transl, of a Japanese news article from the Okinawa Times.)

Teruya was Chief of Ryukyu Inst. of Public Health. In the district of Ryukyu Isle, Yaeyama, and the southernmost part of Japan, *Cycas revoluta* grows well even on barren soil. In these districts the seeds and stems of the plants, which contain large amounts of starch, are an indispensible food for the residents in lean years. It is well known that this plant contains poisonous components and, used without proper treatment, may cause poisoning and even death.

The residents of these islands know by their traditional instruction of the existence of the toxic components and of the method for its removal in preparing safe food in times of shortage. Preparation is tiresome but they do not mind in order to prepare safe food in famine situations. Both seeds and stems are traditionally used in this way and without any trouble with poisoning.

The method learned from Nishida is as follows: the kernels are crushed, dried in the air and sun, ground by a stone mill, and strained through a cheese cloth. The powder is soaked in water overnight and the supernatant is decanted. The residue is washed several times and then boiled. From 100 kg of the kernels, 27 kg of starch are obtained.

Starch was prepared from stems as follows as told by Mr. Miyakuni, the survivor of this fatal accident. (1) The pith of the stem was sliced thin and dried in the sun for 3 days. (2) The dried pieces were soaked for 3 days and then decanted. (3) The residue was dried in the air for a day and packed with zebra grass followed by spontaneous fermentation. (4) After about 10 days the contents were black due to the growth of mold. They were spread in a thin layer and dried in the air but were not washed well after the fermentation and then were used for food immediately.

The fatal accident was due to insufficient drying of pith chips, insufficient drying in the air, insufficient washing after fermentation, and being used for food immediately. On 11 Nov. the family ate cycad gruel for lunch and cycad gruel with corn and rice for supper; on the 12th, they ate cycad gruel with corn for breakfast. Ill at noon, mother and number children died after headache, bellyache, and giddiness followed vomiting and spasm and loss of consciousness, feeble pulse and swollen liver. Mother and all children died by the 14th; the father recovered by the 22nd.

The typhoon in this year caused severe, continued dry weather; the farmers suffered an economic blow because of this, one of their worst harvests ever. Although other villagers used cycads for food, Mr. Teruya had not heard of other poisonings.

Anon.

1957. Letter to M. G. Whiting from a U.S. Coast Guard officer stationed in Okinawa during World War II.

The disease, kinisyukusei-sokusaku kokasho,* exists in Okinawa and has caused some deaths. It is stated that it also causes a condition of the face similar to Bell's palsy.

Cycas revoluta grows here and is eaten as gruel by poorer people when food is scarce. Also they powder the meal and spread it on bread.

From Ie Shima, an island in the E. China Sea in the northern part of Okinawa during World War II: most of the people lost their vision, from a small amount to total blindness. Most of the people were moved off the island; they believed "sotetsu" was the cause of the blindness.

Writer suggests contacting the local hospital: Okinawa Chuo Byoin, Koga, Okinawa.

Hall, W T. K.

1957. Toxicity of the leaves of *Macrozamia* spp. for cattle/Queensland J. Agr. Sci. 14 (2): 41-52 (June).

Moya, E. de Boyrie, M. K. Krestenses & J. M. Goggin

1957. Zamia starch in Santo Domingo: A contribution to the ethnobotany of the Dominican Republic/Fla. Anthropol., Fla. State Univ. 10 (3&4) (Nov.).

Near the end of the 19th century a starch mill was run by water power at the rapids of the Miami River. A few years later one steam-powered mill in present Miami ground 10-15 tons of roots a day. The last mill ceased operation in South Florida in 1925. Goggin in 1938 describes the washing stage practiced by

*Perhaps also spelled "kinshukusei sokumen kokasho"

the Seminóles on the Dania Seminóle Reservation. The plant seems to prefer limestone soils, doing well on the eroded late Pleistocene rocks of South Florida, Yucatan, and the West Indies, and it flourishes on shell mounds of the central Florida west coast.

Standley, P. C. & J. A. Steyermark

1958. Flora of Guatemala/Fieldiana: Bot. 24 (Pt. 1), Chicago Nat. Hist. Mus. P. 16, 18.

Vernacular in Central America: "camotillo," "cocalito."

From text: "The large starchy roots are reported to be used in Peten, (Guatemala) for poisoning rats, and [it] is believed that they have been used many times in Central America for criminal poisoning of human beings."

Theiret, J. W.

1958. Economic botany of the cycads/Econ. Bot. 12:3-41.

This article begins with an excellent review and description of the recognized genera of the Cycadaceae. There follows an extensive description of the potential of each as a food source in regions where it flourishes, with specific directions and precautions that will ensure safe preparation. By this time the reader has a fine appreciation of the value of cycads in an isolated society with limited food resources.

In the 1940's, Baron von Mueller, a chemist, stated that cycads contain a virulent poison that becomes inert or expelled by heat. Ill effects of two types have been reported: (1) an acute irritant effect, following the ingestion of the seed kernels, manifested in man and other animals; and (2) a chronic nervous affection, following the ingestion of cycad leaves or fresh, young sprouts. This is a common ailment in areas where cycads grow on grazing lands. The vernacular names for this progressive paralysis include "rickets" and "wobbles." It is incapacitating and irreversible and is responsible for great losses in cattle country.

Anon.

1960. The eating of cycad/Civil Affairs Act. Ryukyu Islands 8 (2): 191-193.

On Dec. 3, 1959, a report appeared in a Japanese newspaper that people in Miyako (Okinawa) were reduced to eating cycads because of food shortages. With headlines referring to the area as "Cycad Hell," these stories went out to the U.S. and other countries. For centuries the cycad has been an emergency food and, before World War II, the Japanese government encouraged the planting of cycads. The cycad was recognized as a toxic plant; when not properly prepared, it caused illness or

death. Both stem and seeds were used. From the stem, the pulpy middle section surrounding the hard core was stripped from the plant, cut into thin strips, dried in the sun for one week, then wrapped in jute bags for another week and placed in a cool place for another week to ferment until mold appeared. After removal of the mold, the pulp was ready to be cooked and used in soup with rice or made into a substitute for bean paste. Starch from the seeds was prepared in a similar manner; it required 3 weeks to prepare.

Fysh, C. F., K. J. Hodges &L. Y. Siggins

1960. Analysis of naturally occurring foodstuffs of Arnhem Land/*In C. P*. Mountford, ed., Records of the American-Australian Scientific Expedition to Arnhem Land, 2, Melbourne Univ. Press. Pp. 136-139.

Cycas media R. Br. seeds (pounded), raw sample, after soaking for several days in running water: percent edible: 36%; water: 62.8 gm; protein: 4.9 gm; fat: 0.15 gm; carbohydrate: available, 29.0 gm; by difference, 30.8 gm; calories 139 per 100 gm edible portion.

Robertson, E. L.

1960. "Stuffed shirts" raised Coontie/Trop. Living. (Aug).

"Arrow root" (cycad) starch was used to make cookies, crackers, cocoa filler, spaghetti, starch puddings, and more. Indians made bread of cycad starch when they couldn't remain in one place long enough to raise corn. Comptie (cycad starch) was considered sacred.

Webb, L. J.

1960. Some new records of medicinal plants used by the aborigines of tropical Queensland and New Guinea/Proc. Roy. Soc. Queensland 71 (6): 103-110.

In New Guinea, juice and flesh of "nuts" (seeds) of *Cycas circinalis* and powdered kernels of *Cycas media* are applied to wounds.

Dale, I. R. &P. J. Greenway

1961. Kenya Trees and Shrubs/Buchanan's Kenya Estates, Ltd., Nairobi & Hatchards, London. Pp. 2-3.

From text: *Encephalartos hildebrandtii:* "Each scale bears 2 orange-red seeds with fleshy outer and hard inner coats. The Brazil-nut-like kernel after boiling, drying and grinding may be used as flour. The pith of the stem may also be used as famine food. The chopped pith is allowed to stand and ferment for a week, and is then washed in hot water, dried in the sun and pounded up. It may be used as porridge or gruel."

Fix, J.
1961. Anyone for sofkee?/All Florida, TV Week Mag. 11 (4).

"There was a time about 1900 when South Florida Indians (the Seminóles, the Tequestas, and, before them, the Caloosas) controlled the only industry—the production of cooking starch from the roots of *Zamia floridiana*. They prepared a pudding which was a basic ingredient of every meal. The Seminóles called it 'Sofkee'."

Nishida, K.
1961 Study on Azoxyglycosides (from *Cycas revoluta* Thunb.)/Thesis; Japanese Academy of Agriculture. (In Japanese, English transl, of summary.)

Austwick, P.
1962. Toxicity of groundnut meal/Second Conference on Identification of Toxic Elements of Cycads, Aug. 17, Natl. Inst. Health, Bethesda. Pp. 25-44, biblio.

Mr. Austwick, one of the early researchers on this problem, provided an intimate oral and slide presentation of the progress of the investigation since the research on peanuts and *Aspergil-lus* began. Many questions remain unanswered. There are similar problems relevant to the processing and evaluation of cycad toxin(s) in Guam.

Blohm, H.
1962. Poisonous Plants of Venezuela/Harvard Univ. Press, Cambridge. 136pp.

Zamia spp.: This plant is widely known in Central America for its toxic properties, where its roots have been used as a rodenticide. It is believed to have been the cause of many criminal poisonings. Fermentation and boiling are reputed to destroy the toxicity of the roots and render them edible.

Navia, J. M., H. Lopez & R. Harris
1962. Composition of green and ripe cycad nuts *(C. circinalis* L.)/ Dept. of Nutrition and Food Sci., Mass. Inst. Technol., Cambridge.

Findings: "Cycad nuts appear to contain very low quantities of lipid. The lipid content increases about two-fold during ripening. The lipids in the green nut are definitely more unsaturated than the lipids of the ripe nut. A number of unusual fatty acids are present which deserve further study and identification." (See document in document file for data.)

Sokoloff, L.
1962. Multiple exostoses on Guam and lathyrism induced bone tumors/Second Conference on the Identification of Toxic Elements of Cycads, Aug. 17, Natl. Inst. Health, Bethesda, p. 67.

A high incidence of lesions of diaphyseal aclasis is reported in Guam. Two questions remain unsolved: (1) whether the lesions seen histologically in a series of samples are, in fact, lesions of diaphyseal aclasis; and (2) whether lathyrism may be a factor in the pathogenesis of these neurological disorders on Guam. As additional cases accumulate, they will warrant further study.

Watt, J. M. &M. G. Breyer-Brandwijk
1962. Medicinal and Poisonous Plants of Southern and Eastern Africa/E. & S. Livingstone Ltd., Edinburgh and London.

Abstr., p. 370: "The ripe seed of *Encephalartos altensteinii* Lehm, is freely eaten by the baboon and has been eaten with impunity by the Zulu in times of famine. Dr. Rattray has reported that he has eaten them without ill effects and that the Africans in the East London area regard them as edible. He has found that the monkey eats the flesh but discards the kernel. He himself has found that the pulp is not unpleasant but the kernel is astringent like the acorn."

Whiting, M. G.
1962. A bibliography on the chemistry of cycads (family Cycadaceae) from 1900 to 1962/Second Conference on Identification of Toxic Elements of Cycads. Aug. 17, Natl. Inst. Health, Bethesda, Md. Pp. 86-93.

Many of these entries are from the Japanese literature on cycads. Translations are included when available. The list begins with Van Dongen 1903; the earliest Japanese reference is 1918.

Anderson, J. L.
1963. Letter to M. G. Whiting, Feb. 13, 1963. Preparation of cycad seeds for food:

"I have obtained the following information on the use of the seeds of *Cycas circinalis* from the Chief, Division of Botany, Dept. of Forests of this Administration and refers to its use by people near Lae, New Guinea.

"In times of famine when ordinary crops fail, the seeds of *Cycas circinalis* are used as follows: The seed is split in half and the outer skin removed, and then the kernels are soaked in water for 2 or 3 weeks. NOTE: the natives insist that the water must not be changed and that the seeds must 'stink finish' to remove all poison.

"They are then washed, dried, and mixed with shredded coconut if available, formed into cakes, wrapped in banana leaves and cooked on hot stones. More preheated stones are piled on top and the whole covered with banana leaves to steam. It is then eaten either hot or cold.

"Medicinally, the kernels are scraped to a pulp and then used to poultice ulcers, tropical sores, etc."

Anon.

1963. "Zamia Palm." *Cycas media/Northern* Territory Administration (Australia), Animal Industry Branch, 17th Ann. Rep.

P. 26: This widespread plant is a serious problem in areas north of Adelaide River, and it has caused losses in the Darwin/Batchelor area. At times a large percentage of bush cattle appeared to be affected by it. Little control of this plant has been attempted and it flourishes especially after fires. There is no known cure for the paralysis but one dairy farmer claimed that several affected cows improved over a period of time. Consumption of this plant also has affected goats on Groote Eylandt.

Cleland, J. B. &D. L. Lee

1963. The poisonous and urticating plants of Australia/7/í H. L. Keegan & W. V. MacFarlane, eds., Venomous and Poisonous Animals and Noxious Plants of the Pacific Region. Pergamon Press, London.

Gives accounts of explorers affected by ingestion of *Cycas* or *Macrozamia:* (1) Cook's men at Endeavour R. (1770); (2) de Vlamingh and his men ate nuts (1697) and became violently ill, "as dead men"; (3) La Perouse's seamen (1788) had a similar experience at Botany Bay; (4) Mr. Thistle and others of Flinders' complement at Lucky Bay near Esperance; (5) Sir George Grey's men in Western Australia in 1839; and (6) in 1860 some of McDouall Stuart's party sickened on *M. macdonellii.*

Hernández, J. L.

1963. Relación de causa a efecto entre la *Zamia media* y la paresia de los bovinos/Thesis, Univ. Autónoma de Santo Domingo, 45 pp. In Spanish; transl. at Nati. Inst. of Health, Bethesda, Md. (See Innés & Mason 1965.)

This disease has existed for many years in the Dominican Republic, mainly near the coast. A similar paralysis of cattle occurs in Western Australia. In both areas, the disease is thought to be caused by the consumption of *Zamia.* The plant is called "guayiga." Other suspected causes have been investigated, various treatments have been tried, and experts from France and the U.S. Dept. Agr. have been consulted.

In 1922 a consultant, Inspector Frank Hare from the USDA, published a report: Revista de Agr. #4 1922 Dec. 31 Sec. de Industria y Inmigración. Signs occur about 20 days after the plant is consumed. Hernández believes that no other reports exist. He writes of oral information from a beef cattle ranch from another part of the Dominican Republic (probably La

Romana—Ed.) but states he was unable to get information from them.

Laqueur, G. L., O. Mickelsen, M. G. Whiting &L. T. Kurland
1963. Carcinogenic properties of nuts from *Cycas circinalis* L. indigenous to Guam. J. Natl. Cancer Inst. 31:919-951.

Neoplastic disease in rats developed after ingestion of cycad nut meal as a part of the diet. The nuts, obtained from the plant *Cycas circinalis* L., indigenous to Guam, originally were suspected of possessing a neurotoxin. Although the experiments failed to demonstrate this effect, benign and malignant tumors developed, mainly in the liver and kidneys.

Whiting, M. G.
1963. Toxicity of cycads/Econ. Bot. 17 (4): 270-302 (Oct.-Dec).

A review of the literature on the use of cycads as food and medicine with special attention to their toxic properties. In the tropics and subtropics, where the plants are indigenous, their toxicity has long been known. Both gastrointestinal and neurological effects have been reported. Although several toxic components of the plants have been investigated, none has yet been shown to be responsible for specific effects. No lesion has been demonstrated to account for the progressive and apparently irreversible posterior paralysis that reputedly follows consumption of the plants by cattle. Current interest in the toxicity of the cycads has been stimulated by recognition of the high incidence of neurological diseases in an area of the world where they are used for food.

Anderson, J. L. & W. T. Hall
1964. Neurotoxic effects from cycad leaves/Third Conference on Toxicity of Cycads, Fed. Proc. Fed. Amer. Soc. Exp. Biol. 23 (6) (Pt. 1): 1349, plus correspondence.

(1) Description of a feeding experiment with cattle and sheep in New Guinea with findings at autopsy described in correspondence and slides.

(2) Report received by mail describing neurotoxic effects on cattle in Papua New Guinea following the ingestion of cycad leaves. Postmortem findings included.

Campbell, M. E.
1964. Biological effects of the ingestion of the toxic plant *Cycas circinalis* by lab animals/M.S. Thesis, Michigan State Univ., East Lansing.

Dastur, D. K. (with technical collaboration of R. S. Palekar)
1964. Cycad toxicity in monkeys: Clinical, pathological, and biochemical aspects/Third Conference on Toxicity of Cycads, Fed. Proc. Fed. Amer. Soc. Exp. Biol. 23 (6) (Pt. 1): 1368-1369.

Annotation: One of the rhesus monkeys fed chapati pancakes made with cycad flour from seeds of C. *circinalis* for 10 months died of an infectious disease. Autopsy findings showed degeneration of anterior horn cells, degeneration and partial loss of pyramidal neurons of motor cortex with some glial reactions.

Forgacs, J. & W. T. Carll

1964. Toxic fungi from the seeds of *Cycas circinalis* L./Third Conference on Toxicity of Cycads, Fed. Proc. Fed. Am. Soc. Exp. Biol. 23 (6) (Pt. 1): 1370-1372.

Forgacs searched for toxic fungi from fermented cycad starch, meal, sliced endosperm, and refined cycad flour. Specimens were examined macroscopically and microscopically and all were cultured for fungi on a variety of mycologie media at 24 °C.

Fosberg, F. R.

1964. Résumé of the cycads/Third Conference on Toxicity of Cycads, Fed. Proc. Fed. Am. Soc. Exp. Biol. 23 (6) (Pt. 1): 1340-1343.

Author emphasizes importance of preserving voucher specimens whenever and wherever collected.

Hall, W. T. K.

1964. Plant toxicoses of tropical Australia/Aust. Vet. J. 40:176-182.

Innés, J. R. M. (Chairman), M. G. Whiting, L. T. Kurland, J. Cammermeyer, D. K. Dastur, Dr. Yamamoto, R. Harris, G. L. Laqueur, M. Spatz, A. Alien, C. Hoch-Ligeti, Dr. Jubb, J. A. Henderson & C. H. Gallagher

1964. Meeting on Cycad Toxicity with Special Reference to Neurotoxic Properties. Oct. 26, 1964, Bethesda, Md.

Dr. Henderson has been livestock consultant to the Central Romana Corporation, Dominican Republic, for several years and spends about one week every six months on duty on the island. He described in some detail the history of the disease believed to be associated with *Zamia** plant poisoning, locally known as "derriengue." In a total of about 40,000 head of cattle (Brahma), around 500 are affected yearly. Animals do not die, but adult (not young) animals develop what seems to be some neurological disorder resulting in posterior motor weakness, dragging of the hind feet, and occasionally a stringhalt-like action of the hocks. Some attempts have been made to clear pastures of the poisonous plant, and it is said that when this is done, cases do not occur. Because of the difficulty in destroying the plant, the clearance is rather cursory. No systematic work has been done on the pathology of this disease. One report by Dr. Jubb states "There is . . . a widespread loss of myelin sheath associated with odd distortions of the lipoprotein skeleton of the myelin. The axons are also degenerate, being swollen

and variously distorted. These lesions would fit an ascending or descending degeneration from some focal destructive lesion at a different level."

Kingsbury, J. M.
1964. Poisonous Plants of the United States and Canada/Prentice-Hall, Inc., Englewood Cliffs, N. J. P. 123.

Kobayashi, A. & H. Matsumoto
1964. Methylazoxymethanol: The aglycone of cycasin/Third Conference on Toxicity of Cyads, Fed. Proc. Fed. Amer. Soc. Exp. Biol. 23 (6) (Pt. 1): 1354-1356.

Experimental evidence has been obtained to show that MAM and not cycasin per se is the toxic component of *Cycas circinalis.* Results demonstrate that, in spite of its instability, MAM can be isolated, making prospects for its synthesis better than anticipated. Comments received by mail from Riggs (Aust.), Druckery (Germany), and Magee (Engl.) are included.

Kurland, L. T.
1964. Introduction/Third Conference on Toxicity of Cycads, Fed. Proc. Fed. Amer. Soc. Exp. Biol. 23 (6) (Pt. 1): 1337-1339.

At the opening of the Third Conference on Cycad Toxicity, Kurland reviewed the medical basis for our interest in the botanical family Cycadaceae, which grows and is used as food and medicine on Guam. In spite of its known toxicity, cycad starch has been an important food source due to the island's isolation and to typhoons that frequently destroy the local food resources. Other neurological diseases such as Parkinsonism-dementia (P-d) are now recognized as also occurring with high incidence in the Chamorro population. Variations from the usual P-d syndrome will be considered.

Levene, C. I.,S. Duban & R. H. Hughes
1964. Effects of cycasin and cycad meal/Third Conference on the Toxicity of Cycads, Fed. Proc. Fed. Amer. Soc. Exp. Biol. 23 (6) (Pt. 1): 1366-1367.

Cycasin does not appear to be lathyrogenic in the chick embryo. Effects of cycad meal on the guinea pig are discussed.

Miller, J. A.
1964. Comments on chemistry of cycads/Third Conference on Toxcity of Cycads, Fed. Proc. Fed. Amer. Soc. Exp. Biol. 23 (6) (Pt. 1): 1361-1362.

Miller reviews the chemistry of cycads and discusses the comments of Dr. Weiss. A suggestion is made for experiments with diazomethane.

*Genus of cycad commonly found in the Caribbean area including Florida.

Nagahama, T., I. Ijuin & T. Watanabe
1964. Azoxyglycosides occurring in the outer shells of seeds of *Cycas circinalis L./Agr*. Biol. Chem. 28 (8): 573-574.

O'Gara, R. W., J. M. Brown &M. G. Whiting
1964. Induction of hepatic and renal tumors by topical application of aqueous extract/Third Conference on Toxicity of Cyads, Fed. Proc. Fed. Amer. Soc. Exp. Biol. 23 (6) (Pt. 1): 1383.

Aqueous extract of cycad seeds applied to crotón oil-induced ulcers of the skin induced hepatic and renal tumors in C57 BLACK mice.

Weiss, U.
1964. Comments on chemistry of cycads/Third Conference on Toxicity of Cyads, Fed. Proc. Fed. Am. Soc. Exp. Biol. 23 (6) (Pt. 1): 1357-1360.

Whiting, M. G.
1964. Food practices in ALS foci in Japan, the Marianas, and New Guinea/Third Conference on Toxicity of Cycads, Fed. Proc. Fed. Am. Soc. Exp. Biol. 23 (6) (Pt. 1): 1343-1345.

Diet constituents are compared in three areas in the Pacific where high incidence of amyotrophic lateral sclerosis has been reported.

Anon.
1965. The cycads of Guam/Lancet: 593 (Mar. 13).

Among the Chamorros, the indigenous population of Guam and other Mariana Islands, there is a high incidence of amyotrophic lateral sclerosis and parkinsonism-dementia complex. Diaphyseal aclasia, gout, and diabetes also are unusually common in Guam. Interest in this uncommon disease distribution has led to a study of the toxicology of the cycads, an ancient food plant used by many, particularly in Guam and other Mariana Islands.

Preparation of cycads for food is a time-consuming process. The seed is thinly sliced, soaked in water, dried, and then ground into flour.

Attempts to reproduce a neurological disorder by feeding cycad seed meal were successful in only a single animal, a rhesus monkey.

Laqueur et al. have produced a high yield of malignant tumors in experimental animals by feeding them cycad starch.

Innés, J. R. M. & M. Mason
1965. Derriengue investigations in Dominican Republic/Fourth Conference on Toxicity of Cycads, Apr. 15, Natl. Inst. of Health, Bethesda, Md. Pp. 4-39 and appendix pp. 140-165.

Report and discussion of Mason's trip to La Romana, Dominican Republic, during which he made a film of cattle with derriengue paralysis attributed to comsumption of Zamia *[Macro-zamia]* leaves.

Comments by letter from Hall (Queensland) and Gallagher (Sydney) are also included. (See Hernández 1963.)

Riggs, N. V.
1965. Decomposition and carcinogenic activity of azoxyglycosides/ Nature 297:632.

Demonstrates that cycasin and macrozamin may be effective methylating agents in vitro.

Strong, F.
1965. Chemistry of cycads/Fourth Conference on Toxicity of Cycads Apr. 15, Natl. Inst. Health, Bethesda, Md. Pp. 40-76.

Dr. Strong chaired both morning and early afternoon sessions.

Campbell, M. E., O. Mickelsen, M. G. Yang, G. L. Laqueur & J. C. Keresztesy.
1966. Effects of strain, age and diet on the response of rats to the ingestion of *Cycas circinalis/J.* Nutrition 88:115-124.

Cycad flour is similar to refined wheat flour. Young rats seemed to be more severely affected by cycad toxicity than older ones. Strain, sex, and source of animals had no apparent effect on susceptibility. Rats fed 2% cycad diets for 2 weeks died with typical signs of cycad toxicity.

Miller, J. A.
1966. Cycads and cycasin intoxicants occurring naturally in foods/ Publ. 1354, Natl. Acad. Sci., Natl. Res. Council, Wash., D.C. Pp. 30-32.

Adapted: From the roots (and tubers), stems, and fruit (seeds), cycads have provided emergency and staple food for man and animals. The cycads have long been known to contain principle(s) toxic to man and livestock. However, the toxin(s) can be extracted with water.

Recent interest in the cycads developed from the possible relationship of these plant sources of food and medicine to the high incidence of certain neurological diseases in the areas where they are used by the natives. Until recently not much support developed for this relationship. However, these studies revealed a quite unexpected result. When rats were fed the toxic cycad nut meals, several of the animals developed primary tumors in the liver and kidney. Later studies showed that the toxic nut meal is hepatocarcinogenic in the guinea pig and that cycasin is carcinogenic in the rat.

Stanton, M. F.
1966. Hepatic neoplasms of aquarium fish exposed to *Cycas circina*-fe/Abstr. #2670, Pathol., Apr. 11-16. Fed. Proc. Fed. Am. Soc. Exp. Biol. 1966, Mar.-Apr. 25 (2) (Pt. 1). P. 661.

Abstr. : *"Brachydanio rerio* and *Lebistes reticulatus* developed acute degenerative changes in the liver and pancreas after either feedings of cycad meal or the addition of cycasin (methylazoxy-methanol-beta-glucoside) to the tank water. In immature *L. reticulatus,* the 10 day-LD50 following a single dose of cycasin was 22 ppm. The surviving fish possessed only residual fragments of regenerating liver tissue and were relatively resistant to subsequent additions of the water soluble cycasin. Continuous feeding of a 50% dietary supplement of cycad nut meal to *B. rerio* also resulted in acute liver necrosis with subsequent regeneration of poorly organized hepatic tissue. Although normal hepatic structure was lost and hepatic function appeared to be severely impaired, most fish survived and continued to feed on the cycad meal until the termination of the experiment at 44 weeks. Fish killed at intervals during the experiment indicated that foci of hepatic cells of varying stucture develop in the residual hepatic tissue, and that many of these foci have all characteristics of malignant neoplasms. The experiments suggest that aquarium fish are capable of withstanding extreme liver injury from high levels of hepatotoxic agents and may be more sensitive detectors of liver carcinogens than rodents."

Yang, M. G., O. Mickelsen, G. L. Laqueur & J. C. Keresztesy
1966. Irreversibility of damage caused by the ingestion of toxic cycad by rats/Fed. Proc. Fed. Am. Soc. Exp. Biol. 25 (2) (Pt. 1): 2671.

Abstr.: "Kernels from the seeds of *Cycas circinalis* are processed for food by the people of Guam. To determine if the toxic effects resulting from the ingestion of cycad are reversible when the cycad is removed from the diet, rats were fed different levels of unprocessed cycad kernels for varying lengths of time. Characteristic liver damage was absent when rats were fed diets containing 1 or 2% cycad for 5 days followed by feeding a control diet for 10 or 20 days. This was not true when diets contained 3 or 4% cycad. Longer periods following the resumption of the control diet may lead to tumor development . This was suggested when rats were fed a diet containing 2.5% cycad for 13-18 days. Kidney and liver tumors were seen in about 90 and 30% of the rats respectively after 8 months of control diet feeding. In another trial, rats did not reach the same body weight as the control rats, when fed a diet containing 1.5% cycad for two weeks. Weights of the livers of these rats were decreased significantly."

Bell, E. A., A. Vega & P. B. Nunn
1967. A neurotoxic amino acid in seeds of *Cycas circinalis/Fifth* Conference on Cycad Toxicity. Apr. 24-25, Fairchild Tropical Garden, Miami, Fla.

Abstr.: A previously unknown amino acid, alpha-amino-beta-methylaminopropionic acid (meDAP), has been isolated from seeds of *Cycas circinalis* and shown, when injected intraperitoneally, to produce neurotoxic effects in young chicks.

Birdsey, M. R.
1967. Some recent advances in the taxonomy of cycads/Fifth Conference on Cycad Toxicity. Apr. 24-25, Fairchild Tropical Garden, Miami, Fla.

All of the ten genera of cycads and 95 taxa have been assembled in a living collection.

Birdsey described and demonstrated features that separate the genera of cycads and showed the group all ten cycad genera using live material.

The use of these species is available to other investigators on request to the author (Dept. Biol., Miami-Dade Jr. Coll., Miami, Fla. 33156).

Hirono, I. & C. Shibuya
1967. Induction of a neurological disorder by cycasin in mice/Nature (London) 216: No. 5122; 1311-1312.

Authors report that 40 mice (80%), each receiving a single injection of cycasin and surviving for more than 20 days, showed ataxia and posterior paralysis. Gross findings at autopsy were negative. A definite lesion to explain the neurological disorder has not been found.

Inman, N.
1967. Notes on some poisonous plants of Guam/Micronesica 3 (1): 55-66.

"In times of famine cycad seed is prepared as follows: grate or break into pieces and soak for several days in water which must be changed periodically. After a thorough soaking, dry and grind the nuts into meal and bake in thin tortilla-like cakes."

Morton, J. F.
1967. Cycad Uses and Hazards. Morton Collectanea, Univ. Miami, Coral Gables, Fla.

Morton's notable collection of anecdotes and documented materials is well known among both the curious and scientists, for she shares her collectanea graciously. Many of us are indebted to her for the well-documented files.

One example was a letter from "Doc" Fletcher, local wild-plant collector who received information from the Indians, including the Seminóles. For starch, the cycad tubers were scraped or peeled, boiled until soft, then mashed and after the water was poured off, dried in the sun.

For the Indian "sofkee" (stew), the starch was not dried but put into a big pot with more water to which was added venison, coon, turkey, duck, turtle, frogs, alligator tails, ibis, etc. There would also be vegetables such as corn, tomatoes, peas, beans, and whatever else was available. It was cooked slowly and continually until eaten.

Read, R. W.
1967. Taxonomy of the cycads of the West Indies and Florida/Fifth Conference on Cycad Toxicity, Apr. 24-25, Fairchild Tropical Garden, Miami, Fla.

Riggs, N. V. &F. M. Strong
1967. Analysis of cyclitols in cycad plant tissues/Anal. Biochem. 19 (2): 351-356.

Sanger, V., M. G. Yang, O. Mickelsen, M. Mugera & C. K. Whitehair
1967. Species differences in susceptibility to cycad toxicity/Fifth Conference on Cycad Toxicity, Apr. 24-25. Fairchild Tropical Garden, Miami, Fla.

Summary from text: "Unwashed cycad flour was added to the rations of pigs, cows, horses, chickens and rats. In addition ground cycad husk was fed to rats and chickens. The toxic principal in both products produced liver necrosis. Benign and malignant tumors developed in rats which ate either product; the other species did not develop tumors. The toxic principal in the cycad flour passed the placenta in rats and was excreted in the milk of rats, a cow and a sow. In all instances the young animals were affected. No signs of central nervous system disturbances were seen in any of these species."

Vega, A. & E. A. Bell
1967. Alpha-amino-beta-methylaminopropionic acid, a new amino acid from seeds of *Cycas* circinalis/Phytochemistry 6:759-762.

Abstr.: A new basic amino acid, alpha-amino-beta-methylaminopropionic acid, was isolated from seeds of *Cycas circina-lis* and its structure confirmed by synthesis. Preliminary experiments suggest that this compound is neurotoxic to higher animals.

Hall, W. T. K. & M. D. McGavin
1968. Clinical and neuro-pathological changes in cattle eating the leaves of *Macrozamia lucida* or *Bowenia serrulata* (Family *Zamiaceae)/Pathol.* Vet. 5:26-34.

Laqueur, G. L. & M. Spatz
1968. Toxicology of cycasin/Cancer Res. 28:2262-2267 (Nov.).

Mason, M. M. &M. G. Whiting
1968. Caudal motor weakness and ataxia in cattle in the Caribbean area following ingestion of cycads/Cornell Vet. 58 (4): 541-554.

Abstr.: "Ingestion of cycad plant material in Australia, Papua, Puerto Rico and the Dominican Republic has been reported to cause posterior weakness and ataxia, with a characteristic 'goose-stepping' gait in cattle. Six were selected from a group of 25 affected animals in the Dominican Republic. Autopsies were performed with special attention to the removal of the CNS as well as some peripheral nerves. Histological studies were made using H&E, Masson trichrome, Luxol Fast Blue, Pal-Weigert, Bodian and Marchi stains. Only the Marchi stain demonstrated the destruction of myelin around single nerve fibers. The tracts affected were the fasciculus gracilis, dorsal spino-cerebellar, lateral corticospinal, ventral corticospinal, medial longitudinal fasciculus. The lesions were in isolated fibers and were found in the cervical, thoracic and lumbar areas. Two animals affected for less than two weeks had minimal lesions. The four that had symptoms for a month or more showed pronounced lesions. The reversibility of symptoms has not been established. The neurotoxin in the cycad plants has not yet been isolated."

Mugera, G. M. & P. Nderito
1968. Toxic properties of *Encephalartos hildebrandtii/E.* African Med. J. 45:732.

In East Africa the preparation of *Encephalartos* is similar in most parts. In Kilifiahd Lamu districts of Kenya, members of a small tribe known as Wasanya use flour from this plant. They collect the ripe seeds and discard the husks. Seeds are then dried in the sun for one or two days before being ground to a fine flour. This flour, which is red, is used immediately for making porridge ("ugali") and "chapati." It is said that ugali and chapad prepared from this flour are very tasty and keep well for a long time. The preparation of the starch from the seeds is laborious, and the Wasanya do not use it immediately. It is normally kept outside the house and prepared when there is a shortage of food, especially during the dry season when the people are not busy with garden work. It is prepared by breaking off the outer hard shell of the nut, leaving the starchy kernel. The kernel is cut into small pieces, which are then dried in the sun. The pieces are then ground into a white, coarse flour. This flour is placed in a pail of water and the water changed daily for eight days. After this, the coarse flour is dried and ground to a fine powder, which is used for preparation of ugali and chapati. The dry

flour keeps very well and can be stored indefinitely. Ugali and chapati are common foods for most tribes in Kenya and are prepared usually from wheat or maize flour. The Wasanya are unique in using the starchy kernel flour of the cycad for preparation of this type of meal.

The Wasanya know that the kernel and flour, before detoxified with water, are very poisonous. It is believed that all the toxic factors dissolve in water; if animals drink water, they have bloody diarrhea and die within a few days. When man eats improperly prepared starch, gastrointestinal irritation, vomiting, anorexia, diarrhea, apathy, and headache occur. Children get jaundice and die within two to six days.

Silk, S.
1968. Evidence cycad plant can cause cancer in lab animals spurs more research/Natl. Inst. Health Rec. 20 (14): 1,5. July 10. Illustrated.

Informational article with photographs.

Vega, A., E. A. Bell & P. B. Nunn
1968. The preparation of L and D alpha-amino-beta methylaminopropionic acids and the identification of the compounds isolated from *Cycas circinalis* as the L isomer/Phytochemistry 7 (10): 1885-1887.

An improved method for the synthesis of D- and L-alpha-acetaminobeta-methylaminopropionic acid and the use of this compound for the synthesis of the two optical isomers of alpha-aminobeta-methylaminopropionic acid are described. The amino acid previously isolated from seeds of *Cycas circinalis* has been identified as the L-isomer. Unlike the natural amino acid and the synthetic L-isomer, the D-isomer failed to produce toxic effects when injected in comparable amounts into chicks and young rats.

Wells, W. W.,M. G. Yang,W. Bolzer & O. Mickelsen
1968. Gas-liquid chromatographic analyses of cycasin in cycad flour/ Anal. Biochem. 25:325-329.

Summary: "A method for the quantitative determination of cycasin from cycad flour by gas-liquid chromatography is described. The flour is extracted with 70% ethanol and the residue from the dried extract is directly trimethylsilylated. Androsterone was found to be an excellent internal standard. The average content of cycasin from ten separate analyses of one lot of flour was 0.429 gm/100 gm. The method is rapid, sensitive, and not hindered by contaminating compounds."

Yang, M. G. &O. Mickelsen
1968. Cycad husk from Guam: Its toxicity to rats. Econ. Bot. 22 (2): 149-154.

Findings: Feeding husk of *Cycas circinalis* to rats "produced an elevation of packed cell volume and hgb. Fluid was found in abdominal and thoracic cavities at autopsy. Hemorrhages occurred in the gastrointestinal tracts."

Note: The actual amount of cycad husk eaten and swallowed by Guamanians may have been small. Perhaps it was merely chewed and not swallowed—Ed.

Anon.
1969. "Coontie [cycad] pineapple pudding made best with cornstarch. . ."/Coral Gables Times, Coral Gables, Fla., Nov. 27.

First, the tuber was pounded to a pulp, which was washed in running water to remove the toxic ingredients. Further refinement involved the use of screens or sieves or "settling tanks." After the tanks were drained, the white granular starch was dried on racks or trays. Another description mentions that, after the straining process, the starch was put into barrels to be washed again three times while stirring and settling. "… It was allowed to reach the bubbling stage in fermentation for then all the dirt and sugar came out."

Hardin, J. W. & J. M. Arena
1969. Human Poisoning from Native and Cultivated Plants/Duke Univ. Press, Durham, N. C. 167 pp.

"The fleshy seeds (of cycads) are poisonous if eaten in quantity. Paralysis and death have occurred from eating the seeds of *Cycas circinalis* ('fern palm,' 'false sago palm,' 'crosier cycas'). The seeds and roots are used for food in some areas but the alkaloid is washed out first."

For the physician, recommended treatment: gastric lavage or emesis (i.e., "symptomatic").

Hirono, I., C. Shibuya & K. Hayashi
1969. Induction of a cerebellar disorder with cycasin in newborn mice and hamsters/Proc. Soc. Exp. Biol. Med. 131:593-599.

From summary: A single administration of cycasin, beta-D-glucosyloxyazoxymethane, was given in dosage near the LD50 level to newborn mice and hamsters within 24 h after birth. Under these conditions cycasin produced a distinctive neurologic disorder. In the affected newborns there was rapid and extensive necrosis of the cells of the external granular layer (embryonal layer) of the cerebellum. In animals surviving to maturity this resulted in defective development of the molecular and granule cell layers. The affected animals had ataxia and

gait disturbances. Comparable administration of cycasin to rats within 24 h after birth produced no apparent disorder of the central nervous system.

Sanger, V. L., M. G. Yang & O. Mickelsen

1969. Cycad toxicosis in chickens/J. Natl. Cancer Inst. 43 (2): 391-395.

After groups were kept on their respective diets of different cycad content for 14 days, 28 weeks, and 68 weeks, no chickens had tumors attributable to cycads, nor did any have clinical signs of cns disturbances.

Zellermayer, D.

1969. "Pioneer's coontie pie highlights culinary history of Coconut Grove"/Coral Gables Times, Coral Gables, Fla., Nov. 24.

Coontie (pronounced "cumptie") (Seminóle). The starch industry flourished until the 1920s, but plants took up to 30 years to mature and the industry died out when the natural supply was exhausted. The "coontie grounds" near the Cutler and Miami areas furnished an abundant supply. The rootstocks were scraped or peeled; then pounded, grated, ground, or boiled until soft, and then mashed; washed with plenty of water; the drained and the resultant starch dried in the sun. Early settlers operated small coontie mills. The red water running off in the washing process was fatally poisonous to cattle. To make "sofkee" stew, instead of drying the mash, the Indians cooked it with game and vegetables. The preparation process is similar to that used by American Indians in pre-Columbian times when cooking with the poisonous cassava *(Manihot esculenta),* which has long been cultivated commercially as the source of tapioca.

Gardiner, M. R.

1970. Chronic ovine hepatosis following feeding of *Macrozamia reidlei* nuts/Aust. J. Agr. Res. 21:519-526.

Due to the author's interest in hepatotoxins, his lab was available for studying in detail the chronic effects of seeds of *Macrozamia reidlei* on a small number of sheep over a period of 1-11 months.

Hirono, I., H. Kachi & T. Kato

1970. A survey of acute toxicity of cycads and mortality rate from cancer in the Miyako Islands, Okinawa/Acta Pathol. Jap. 20: 327-337.

Included in this cancer survey is a section on consumption during a food shortage period in October, November, and December 1959 and in the first half of January 1960. In the study 1,260 families ate cycad starch; 903 families prepared the starch for this period. Preparation was as follows: "Cycad stem was

barked, cut into slices and sufficiently dried in the sun for 7 to 10 days, then immersed in water to remove the harshness for two days. Slices were taken out of the water, excess amount of water was removed and they were decomposed being wrapped with miscanthus until they heat and become soft. Finally, slices thus prepared were washed a few times with water and boiled with seasoning, known as ojiya, a kind of gruel boiled with bean paste or soy." According to the journal, this population group was recorded so that each person could be located at a later date.

Holz, P.

1970. Cycads: Living relics/S. African Panorama, May: 30-33.

Twenty-six of thirty-five species of *Encephalartos* occur in S. Africa. These cycads are protected under the plant protection ordinances of the various provincial administrations. Many fine specimens have been used to adorn streets in various municipalities and many more are found in public and private gardens. More than 4,000 *E. lebomboensis* were rescued recently through "Operation Wild Flower" from the area to be flooded by construction of the Jozini Dam across Pongola Poort, E. Transvaal. The plant's kernel or endosperm surrounding the embryo has proved poisonous in all species of *Encephalartos* and this suggests that the toxicity of the kernel—shunned by animals—has also had a significant bearing on the persistence of the family through the ages.

Rao, L. N.

1970. Life history of *Cycas circinalis*—G Part 4/Proc. Indian Acad. Sci.,Sect. B. 72(4): 179-186.

Forgacs, J.

1971. Mycologie and myco-toxic examination of *cycads/In* I. F. H. Purchase, ed., Mycotoxins in Human Health. Symposium. Pretoria, S. Africa, Sept. 2-4, 1970. Macmillan, London. xxxiv + 306pp., illus., map.

Goodale, J. C.

1971. Tiwi wives. A study of the women of Melville Island, North Australia. pp. 152, 168, 173, 180-181, 213, 323. University of Washington Press, Seattle, Paperback WP-73.

A type of cycad called "korka" is most common. "Nuts" (seeds) ripen in mid-August, halfway through the dry season. The other type, known as "ignala," is taller and not so widely distributed. Preparation of both was the same. The seeds were gathered from the ground and trees. Women filled a 50-lb bag in about half an hour. A large fire was made; when this had died down, the seeds were placed in a single layer in the hot ashes. During the half-hour cooking time, hot ashes and sand were

gently stirred and mixed with the seeds. Seeds were removed and cooked usually overnight. They were then cracked with a single blow of a heavy iron wood mallet, and the kernel was removed and crushed with a single blow. The crushed seeds were then taken to the freshwater swamp where a "cage" of cycad leaves had been constructed by "planting" them upright in a ring to "keep them [seeds] from running away." They were left for two or three days, then removed and eaten with no further preparation.

Cycad seeds are not a favorite food. Ceremonial use is described on page 181. They are not considered a medicine, either "real" or "magical."

Stone, B. C.
1971. America's Asiatic flora: The plants of Guam/Amer. Sci. 59: 308-319.

Dossaji, S. F. &G. A. Herbin
1972. The occurrence of macrozamin in the seeds of *Encephalartos hildebrandtii.* Sixth Conference on the Toxicity of Cycads. 31 (5): 1470-1472.

From abstr.: "A water-soluble hepato-toxin has been isolated from the seeds of *Encephalartos hildebrandtii* (Cycadaceae) and identified as macrozamin, methylazomethanol-beta-primeveroside.

"Alpha-amino-beta-methylaminopropionic acid reported to be present in the seeds of *Cycas circinalis* (Cycadaceae) was not detected in either the seeds of *Encephalartos hildebrandtii* or the leaves of *Cycas thuarsii.* "

P. 1470: "In Kenya the seeds of *E. hildebrantii* are used by the Wasanya tribe as a source of edible starch during times of famine or whenever there is a shortage of food. The Wasanya are aware of the presence of a toxic ingredient in the seeds, which is removed by steeping the cut, sun-dried, seeds in water for eight days, the water being changed daily. This treatment removes the water-soluble toxin and the seeds are then dried, powdered and used in the preparation of a porridge."

Hirono, I.
1972. Natural carcinogens: Present use of *Cycas revoluta* on Amami Oshima Island/Jap. J. Clin. Med. 30 (4): 924.

A chromatographic study of soy bean paste made from grains and cycads grown in Amami Oshima, Japan, revealed the presence of cycasin, a carcinogen.

Kobayashi, A.
1972. Cycasin in cycad materials used in Japan/Fed. Proc. Fed. Am. Soc. Exp. Biol. 31 (5): 1476-1477

Nishida's experiments 35 years ago satisfied consumers that miso made with cycad seeds was safe to eat. When it became known that cycads were carcinogenic, further analyses were demanded.

Conclusions: Starch and cycad gruel contained hardly any extractable materials and were shown to be completely cycasin-free by all methods of analyses.

"Cycad toys are, of course, not foods. But people, especially babies, may play with them without knowing their toxicity. These toys resembling small dolls are painted or lacquered. One kind, not commercially available, was prepared from cooked kernels of carefully hulled cycad seeds. This toy contained 0.37% cycasin by polarography and 0.21% by gas chromatography. Two other toys were made from raw seeds and when first prepared should have been expected to have a high content of cycasin. However, there was no cycasin in them largely due to the method of preparation. The kernels were cut with a knife which contaminated them with molds that completely destroyed the cycasin and sugars. These moldy samples showed a polarogram similar to that of one of the bean pastes. The absence of cycasin was confirmed by the lack of change in the polarogram after alkali treatment."

Kurland, L. T.
1972. An appraisal of the neurotoxicity of cycads and the etiology of amyotrophic lateral sclerosis on Guam/Fed. Proc. Fed. Am. Soc. Exp. Bio. 31(5): 1540.

O'Gara, R. W. & R. H. Adamson
1972. Spontaneous and induced neoplasms in nonhuman primates/In R. N. T. W. Fiennes, ed., Pathology of Simian Primates, I, Karger, Basel. Pp. 190-238.

From text p. 228.: "Cycasin, an ingredient of the cycad nut and a probable contaminant of human food in several parts of the world, was fed to monkeys for several years. This chemical causes carcinomas of the liver, kidney, and intestinal tract in rats, but so far has not been responsible for any tumors in primates.

Toxic effect differs from that of aflatoxin inasmuch as the necrosis is not as specific for the centralobular area and there is less proliferation of pseudotubules."

Polsky, F. I., P. B. Nunn & E. A. Bell
1972. Distribution and toxicity of alpha amino-beta-methylamino propionic acid/Fed. Proc. Fed. Am. Soc. Exp. Biol. 31 (5): 1473-1475.

Abstr. : Alpha-amino-beta-methylaminopropionic acid either in free or bound form was present in the seeds and leaves of all species of *Cycas* analyzed. A survey of other members of the Cycadales has shown that this "unusual" amino acid may also occur in free or bound form in species of *Lepidozamia, Macrozamia, Encephalartos, Dioon, Zamia,* and *Bowenia.* The concentration of this amino acid in the plants was low, and it is unlikely that it is a major factor in the development of neurological disease in man. At higher concentrations, however, the amino acid is toxic to animals.

Dossaji, S. F. & E. A. Bell

1973. Distribution of alpha-amino-beta-methylaminopropionic acid in Cycas/Phytochemistry 12:143-144.

Abstr.: Alpha-amino-beta-methylaminoproprionic acid, previously isolated from seeds of *Cycas circinalis,* has now been identified either free or bound in all the other nine species of this genus.

Wesley-Smith, R. N.

1973. Cycads and cattle in the Northern Territory/J. Aust. Inst. Agr. Sci., p. 233-236 (Dec.).

Varied results are produced from attempts to eradicate the cycad in pasture land and from feeding cycad fronds to cattle. Emus seem to be resistant to the toxic ingredient of cycads. They eat the seeds with no ill effects. Feeding cycad fronds to cattle failed to produce cycad paralysis consistently. Rotating cattle between cycad-infested and cycad-free ranches has prevented further outbreaks on one project near Darwin. Trials over an eight-year period with a variety of chemicals and with different times of application produced varied results. Removal of the apex of the plant stimulated suckering, thus producing more plants than before eradication. The author believes that new methods and materials are now available to allow eradication of the cycad at moderate cost.

Altenkirk, B.

1974. Occurrence of macrozamin in the seeds of *Encephalartos transvenosus* and *E. lanatus/Lloydia* 37 (4): 636-637.

Chemical tests and animal experiments reported (S. Africa).

Hooper, P. T., S. M. Best & A. Campbell

1974. Axonal dystrophy in the spinal cords of cattle consuming the cycad palm, *Cycas media/Aust.* Vet. J. 50 (4): 146-149.

From text: *Cycas media,* commonly known as "zamia palm," is a serious hazard to the cattle industry of the Darwin area. Its consumption by cattle and goats causes ataxia and paralysis of the hind limbs (Hall 1964), a condition locally called "rickets" or "wobbles."

This paper reports the neuropathological findings from three steers affected by C. *media* poisoning.

Kobayashi, A., M. Toya, R. Fukunishi & A. Yoshida
1974. Safety evaluation of sotetsu-miso, cycad bean paste; chemical determination of toxic substances and long-term feeding tests of the miso/Abstr. Intl. Symp. Chem. Natl. Prod., Intl. Union Pure and Appl. Chem., Kyoto, Japan. 6:263-268 (Apr. 27).

Cycasin was assumed to be hydrolyzed due to beta-glucosidase in the cycad seeds and was not detected in the air-dried seeds or in cycad flour prepared in the usual way as the raw material of the miso. Cycad flour prepared from heated cycad seeds still contained cycasin. The growth of the mold *koji* (starter culture) was suppressed on a mixture with this flour, and hence *koji* of good quality was not obtained. Cycasin was, however, destroyed in the early stage of *koji-making* in this experiment. There was no evidence of toxicity to rats . . . no aflatoxin was found in *sotetsu-miso* either raw, home-made, or commercial.

Tustin, R. C.
1974. Toxicity and carcinogenicity of some South African cycad *(Encephalartos)* species/S. African Med. J. 48 (57): 2369-2374.

The carcinogenicity of four species of S. African cycads is reported for the first time.

Van Houten, L.
1974. Health and medicine in Guam and Micronesia: A bibliography/ Medical Library, Guam Memorial Hospital, Tamuning, Guam. July 1974. Typescript, 22 p.

Forty-two references on amyotrophic lateral sclerosis and eight references on parkinsonism-dementia.

Yokoi, S.
1974. Wild edible plants used by Mr. Shoichi Yokoi in Isle of Guam. Personal narrative in Japanese. (Hamilton Libr., Univ. Hawaii, Honolulu. PAC D811.Y55 A32.)

Mr. Shoichi Yokoi, a soldier in the Japanese army stationed in Guam during World War II, not knowing the war was over, stayed for two years in the jungles of Guam after the war ended. He prepared cycad seeds but did not like them so did not eat many. (See also Kahn, E. J., Jr. 1962, The Stragglers/The New Yorker 47-121 March.)

Gabbedy, B. J., E. P. Meyer& J. Dickson
1975. Zamia palm *(Macrozamia reidlei)* poisoning of (young) sheep/ Aust. Vet. J. 51:303-305

Summary: Sheep mortality caused by the ingestion of leaves of the *Zamia* palm *(Macrozamia reidlei)* were recorded from six properties in Western Australia from 1966 to 1971. Deaths

occurred in sheep less than two years of age and involved from two to nine percent of the flock. The primary lesion was acute hepatic necrosis; neurological effects were not recorded. The condition was reproduced experimentally when crushed kernel, macerated leaf, or leaf extract was administered by stomach tube.

No paralysis is recorded—Ed.

Louw, W. K. A. & W. Oelofsen

1975. Carcinogenic and neurotoxic components in the cycad *Encephalartos altensteinii* Lehm. (Family *Zamiaceae)/Toxicon* 13:447-452.

Abstr.: "Evidence is presented for the existence of an apparently macromolecular component(s) possessing neurotoxic properties. Aqueous extracts from seeds of *Encephalartos altensteinii* were passed through an Amicon UM-2 ultrafiltration membrane with a general molecular mass retentivity of 1000. The retentate produced neurotoxic symptoms when administered to guinea pigs. Macrozamin (methylazoxymethanol-beta-primeveroside), a potent carcinogen, was isolated from the diffusate, and after purification by means of adsorption on charcoal and ion-exchange chromatography, was obtained in crystalline form."

Beatón, J. M.

1977. Dangerous harvest/Unpubl. Ph.D. Thesis, Australian Natl. Univ., Canberra.

Approximately one third of this dissertation concerns species of the plant family Cycadaceae, native to Australia, especially the precise directions for their preparation for food. Charred remains found in caves provide evidence of its use as a staple, for ceremonials, and as a communal food; carbon dating is 4000 to 5000 B.C. The Aborigines are alert and knowledgeable regarding toxicity and the precautions necessary. They also can identify seeds lying on the ground that are already detoxified, which can be eaten without further processing.

Beatón has included numerous tables and charts that document his observations on length of time, month, and season for harvesting, which is carefully calculated and supervised by the elders. Field animals choose different parts of the plant for food. For example, some were observed to eat the husks rather than the kernels at certain times of the year.

Note especially the description of an encounter with Aborigines during the cycad harvest and seed processing by Meehan & Rhys (1977) below.

Buckley, R. T., Jr.
1977. The cultivation and propagation of cycads/Amer. Hort. 56 (3): 22-25, 29.

An informative article about the cultivation and propagation of cycads. Includes listing of the cycads commonly offered by mail-order nurseries.

Egoff, R. C.
1977. The cycads (Cycadaceae), the nuts that dinosaurs ate. *In* E. Menninger, ed., Edible Nuts of the World, Ch. 28, pp. 161-164.

This chapter describes the evolution of the cycads during the Mesozoic era when dinosaurs ruled the earth. Cycads are described as long-lived and hardy, providing emergency food after proper detoxification.

Laqueur, G. L.
1977. Oncogenicity of cycads and its implications. *In* H. J. Kraybill & M. A. Mehlman, eds., Advances in Modern Toxicology 3. John Wiley & Sons, N. Y. Ch. 7, pp. 231-261.

Meehan, B. & J. Rhys
1977. Preliminary comments on the preparation of *Cycas media* seeds by the Gidjingali of Coastal Arnheim Land. *In* J. M. Beatón, ed., Dangerous Harvest. Unpubl. Ph.D. Thesis, Australian Natl. Univ.

Meehan and Rhys describe in detail their experiences on a cycad seed collection trip with the Gidjingali on the north coast of Arnheim Land in July and August 1977. A common water hole was used for soaking by three related groups. One or two seeds from a potentially acceptable tree were tested on the spot by being cracked open. If judged to be "ready," then the whole tree was stripped. If the women could not reach the top branches, they either climbed the tree by cutting wedges in the trunk or they cut it down.

When a load (15 kg) was collected, it was carried to the daytime camp and the dehusking began.

At lunch [damper (a common Australian breadstuff) and tea and a pipe or two] people were extremely fussy about having clean hands.

Collecting and dehusking continued for about seven days. The seeds were placed on a flat object and each crushed into several pieces, which were placed in a porous container that was immersed in clear water for about seven days. The water had by then become a seething mass of white froth and bubbles rising almost to the top of the hole. The starch was well drained, shaped into loaves, then wrapped in paper bark and baked on a bed of embers. This procedure was repeated at least once.

Cycads are an important food resource for a number of traditional societies living in the tropics, including Australia. Cycads are also in a special food category due to their extreme toxicity, only recently identified.

There could be serious food shortages in some of these areas if it were not for an abundance of cycad starch. Little is known about the natural productivity of cycads, but fire appears to be an effective way of increasing productivity.

A limited experiment was carried out by Beatón on two small groves of cycads, one of which was burned by one of the frequently recurring fires in the area. The other was not burned. The difference in production between the two plots was dramatic. The burned plot produced more than seven times the number of seeds than the unburned plot. Only one tree had two seed cones on the unburned plot, while one tree on the burned area had 27. Further research and observation are planned. Such a dramatic increase would add greatly to the security of a population of Aborigines. It is important that supplies be ample for the ceremonials held at intervals, which help maintain the integrity and cohesiveness of the larger group.

Kurland, L. T. & C. A. Molgaard

1982. Guamanian ALS: Hereditary or Acquired? *In* Lewis P. Rowland, ed., Human Motor Neuron Diseases, Raven Press, N. Y. Pp. 165-171.

From text: "In summary, the evidence at this time favors an exogenous rather than a genetic factor for the development of ALS on Guam. Continued research in three areas should help to produce definitive conclusions. These areas are: (a) continued follow-up of the population on Guam and the other Mariana Islands; (b) epidemiological field research in the Ilocos provinces of the Philippines, and (c) further epidemiological information and pathological confirmation from the New Guinea (West Irian) field site, where the incidence rate is high, and where cases in their 20s and 30s are not infrequent in a demarcated geographic area similar to that noted in the Marianas 30 years ago."

Seawright, A. A.

1982. Chemical and Plant Poisons in Animal Health in Australia, Vol. 2/Aust. Govt. Publ. Serv., Canberra. Pp. 37-38.

Although cycads have a long history of toxicity to man and animals, some have been and still are used as food or medicine in various parts of the world. The relevant literature was reviewed by Whiting (1963: Tables 1-5). Reports of toxicity in animals described an acute condition and are characterized by jaundice, liver injury, anemia, and hemorrhage, and a chronic condition

showing a peculiar paralysis of the hindquarters that appears to be progressive and irreversible. The acute condition usually follows shortly after ingestion of the plant material; the chronic condition appears within a few weeks or a month.

P. 37: "Cycads are probably all toxic for livestock although many are not accessible to grazing animals and accordingly have not come under suspicion as toxic plants. Cycads that have been examined all contain glycosides of methyl-azoxymethanol (MAM), either cycasin or macrozamin. These compounds are not intrinsically toxic but are readily hydrolysed in the alimentary tract, mainly the rumen, to the aglycone MAM.

P. 38: "The condition seen classically in cattle is posterior ataxia, known as 'zamia staggers.' This condition can be produced in sheep, but appears only rarely under natural conditions (Gardiner, 1970). Cycad plant tissues often contain the neurotoxic amino acid, alpha-amino beta methylamino propionic acid but this compound is almost certainly not the cause of 'zamia staggers.' "

Murdock, G. P., C. S. Ford, A. E. Hudson, R. Kennedy, L. W. Simmons & J. W. M. Whiting

1983. Outline of World Cultures./6th rev. ed., Human Relations Area Files, Inc. (HRAF), New Haven, Conn. 259 Pp.

This HRAF manual provides a place for data on every known society including prehistoric peoples. It is invaluable for cross-cultural research. Index included.

Beck, Wendy

1985. Technology, toxicity and subsistence: A study of Australian Aboriginal plant food processing/Unpubl. Ph.D. Thesis, Div. of Prehistory, School of Humanities, La Trobe Univ., Aust.

Beck investigated the Australian hunter-gatherer subsistence diet and its preparation, especially the removal of toxic, unpalatable and indigestible substances found in Australian plant foods. A cycad, *Cycas angulata*, contains large quantities of edible starch suitable for providing several days' food supply for communal gatherings. The Aborigines have long known of the toxicity of this plant and of its occasional side effects: nausea, vomiting, and mild to serious illness and, occasionally, death. When chemists identified the toxin cycasin, Beck designed field tests for estimating the toxicity before and after processing.

Beck observed natives separating (and sometimes discarding) seeds on the basis of tactile and visual inspection and olfactory clues. To the outsider, the Aborigine seemed casual about his selection of "safe to eat" seeds from among those lying on the ground; such seeds were often picked up and eaten without fur-

ther treatment. Length of time for leaching varied according to the age and condition of the seed. Three levels are considered: a long leaching period of several months, a short leaching period of a few weeks, and no leaching.

Kono, I., E. Takehara, T. Shimizu, N. Yasuda, A. Kobayashi, K. Tadera & F. Yagi

1985. Experimental studies on effects of cycasin on guinea pigs. Bull. Kagoshima Fac. Agr. Kagoshima Univ. 35:159-170. (In Japanese, with English summary.)

Results: Signs of toxicity of cycasin in guinea pigs are very similar to those reported in other experimental animals. No neurological signs were observed.

Yasuda, N., I. Kono &T. Shimizu

1985. Pathological studies on cycad poisoning of cattle experimentally caused by feeding with leaves of cycad: *Cycas revoluta.* Bull. Kagoshima Fac. Agr., Kagoshima Univ. 35:171-178. (In Japanese, English summary.)

Annotation: Two cows were fed leaves of *Cycas revoluta.* Signs of dyskinesia in hind quarters were observed in one animal at 36 days and at 82 days in the other. A temporary increase in serum gamma-GTP level was observed immediately after cycad leaves were ingested. Microscopic examination showed vacuolation and fibrillary gliosis in the spinal cord, which the observers considered to be due to cycad poisoning.

Calne, D. B., A. Eisen, E. McGeer & P. Spencer

1986. Alzheimer's disease, Parkinson's disease, and motoneurone disease: Abiotropic interaction between ageing and environment?/ Lancet: 1067-1070 (Nov. 8).

Summary from p. 1067: "The hypothesis is that Alzheimer's disease, Parkinson's disease (PD), and motoneurone disease are due to environmental damage to specific regions of the central nervous system and that the damage remains subclinical for several decades but makes those affected especially prone to the consequences of age-related neuronal attrition. This proposal is based on the association between environmental factors and certain neurodegenerative diseases . . . and on the long latent period between exposure to environmental factors and the appearance of symptoms in some of these disorders. The practical implications of this hypothesis are that (1) epidemiological attention should be focussed on the environment in early rather than late life, (2) prevention may be a realistic goal if the cause of subclinical damage can be identified, (3) a search should be undertaken for causal mechanisms linking subclinical neuronal damage due to an environmental factor and the normal ageing process, and (4) better understanding of the regional selective

vulnerability of the nervous system to the ageing process might allow a rational approach to treatment."

Guam (p. 1070): "A degenerative neurological disorder of unknown cause and characterised by motoneurone disease, parkinsonism and/or Alzheimer-type dementia (the amyo-trophic lateral sclerosis [ALS]-PD complex) used to be common in Guam, where the prevalence of motoneurone disease in 1960 was at least fifty-fold higher than in either Europe or North America. The ALS-PD complex also occurs in Southern New Guinea (Irian Jaya) and the Kii Peninsula of Japan. Morphologically, lesions are found in upper motor neurons, lower motor neurons, the substantia nigra, the hippocampus, and the medial basal forebrain. Calcium and magnesium deficiency leading to accumulation of aluminium and/or consumption of a cycad seed containing an amino acid, beta-N-methlyamino-L-alanine (BMAA), have been suggested as causes of the ALS-PD complex.

"The following points are pertinent to our hypothesis—(1) the disease is of environmental origin and is disappearing as the Guamanian life-style becomes westernised; (2) in subjects reared in Guam who leave the island in early adult life the disease may develop up to 34 years after emigration; (3) once clinically manifest, the course of the disease is commonly fulminant, with death occurring in 5 years; (4) neurofibrillary tangles are found, as in several other abiotrophic disorders; (5) a well-documented increase in tangles has been reported in some symptomless Guamanians, a finding suggestive of subclinical damage."

Garruto, R. M. & Y. Yase

1986. Neurodegenerative disorders of the western Pacific: The search for mechanisms of pathogenesis/Trends Neurosci. 9:368-374.

Abstr. From the text: "The systematic search for etiological factors and pathogenetic mechanisms of neurodegenerative disorders is perhaps nowhere better exemplified than in the western Pacific. During the past three decades, the opportunistic study of high incidence amyotrophic lateral sclerosis and parkinsonian syndromes has occurred in relatively remote, isolated regions where numerous confounding genetic, cultural and environmental variables, found in larger cosmopolitan communities, do not occur. These unique foci have already greatly enhanced our understanding of contemporary problems in the neurobiology of disease and hold further promise for new avenues of investigative research in the years to come."

N.B. To date these authors have found no association between ALS and PD and plant and animal toxins despite research on

the cycad *(Cycas circinalis),* cassava, and fish poisons on Guam—Ed.

Spencer, P. S., P. B. Nunn, J. Hugon, A. Ludolph & D. N. Roy
1986. Motor neurone disease on Guam: Possible role of a food neurotoxin/Lancet: 965 (Apr. 26).

Guam Island of the western Pacific has a very high incidence of amyotrophic lateral sclerosis-parkinsonism dementia (ALS-PD). The cause remains unknown. An environmental agent is considered likely, since incidence has fallen since the life-style became more westernized. Attention is now focused on the effects of an amino acid naturally present in cooking starch from a local food plant *(Cycas circinalis* L.). The authors' preliminary studies show that administration to male cynomolgus monkeys induces a degenerative motor-system disease.

Spencer, P., J. Hugon, A. Ludolph, P. Nunn, S. Ross, D. Roy, H. Schaumburg & A. Soiefer
1986. Primate motor-system disease induced by beta-N-methylamino-L-alanine in cycad. *Cycas circinalis* seed a suspect etiologic agent of Guam amyotrophic lateral sclerosis/parkinsonism-dementia/J. Neuropathol. Exp. Neurol. 45:358. (Conf. paper.)

Anon.
1987. Toxic seeds and degenerative diseases/Science 237:471.

From text: "Indigenous peoples of Guam and Rota, the Chamorros, once had a high incidence of amyotrophic lateral sclerosis, parkinsonism, and Alzheimer-type dementia (the syndrome ALS-PD). . . . Since World War II, the incidence has progressively declined. Genetic factors and viral agents have been ruled out as causes of ALS-PD, and explanations have been sought in changing cultural practices resulting from Americanization.

"Toward the end of World War II, the Chamorros had to rely heavily on *Cycas circinalis*—the false sago palm seed—for food and medicine. The seeds contain an unusual toxic amino acid, called L-BMAA. When synthetic L-BMAA was fed to macaques, Spencer et al. found that cells of the nervous system underwent structural and functional changes, and motor disfunctions, and behavioral changes like those seen in motor neuron diseases and parkinsonism were induced. These findings suggest an explanation for the hitherto enigmatic clustering of symptoms and lend support to the hypothesis that toxic amino acids (in this case from a source outside the body, but in other cases possibly from an endogenous source) may be associated with development of parkinsonism, Alzheimer's and perhaps other degenerative diseases. . . ."

Hall, W. T. K.
1987. Cycad (zamia) poisoning in Australia/Aust. Vet. J. 64 (5): 149-151.

Cycads were the subject of the first documented plant poisonings in Australia when Captain Cook's men and their pigs were affected by eating cycad seeds (1770). In 1847, Leichardt reported that the aborigines, after they had given the seeds a good soaking, tied them up closely in tea tree bark to "undergo a peculiar process of fermentation."

Lewin, R.
1987. Environmental hypothesis for brain diseases strengthened by new data/Science 237:483-484.

"A combination of dogged determination and inspired science appears to have solved the mystery of a brain disease on Guam and adds fuel to a controversial hypothesis in neurology."

Nunn, P. B., M. Seelig, J. C. Zagoren & P. S. Spencer
1987. Stereospecific acute neuronotoxicity of 'uncommon' plant amino acids linked to human motor-system diseases/Brain Res. 410:375-379.

Abstr.: "The L-isomer of beta-N-methylamino-L-alanine (BMAA), present in free form in seed of *Cycas circinalis*, elicits in spinal cord cultures a pattern of acute postsynaptic neuronal vacuolation comparable to that induced by beta-N-oxaly-lamino-L-alanine (BOAA), an excitotoxic amino acid of greater potency isolated from seed of *Lathyrus sativus.* The neurono-toxic properties of these compounds may be linked to the etiology of motor-system degenerative disorders (amyotrophic lateral sclerosis and lathyrism, respectively) found in human groups that have used these plant seeds for food."

Ross, S. M. &P. S. Spencer
1987. Specific antagonism of behavioral action of "uncommon" amino acids linked to motorsystem diseases/Synapse 1: 248-253.

Abstr.: "Beta-N-methylamino-L-alanine (BMAA), [and] Beta-N-oxalylamino-L-alanine (BOAA) are chemically related amino acids present in the seeds of *Cycas circinalis* and *Lathyrus sativus*, respectively. Consumption of these seeds has been linked to Guam amyotrophic lateral sclerosis (BMAA) and lathyrism (BOAA; a form of primary lateral sclerosis). A single large dose of BOAA or BMAA causes seizures in newborn mice and postsynaptic neuronal edema and degeneration in CNS explants. . . . Taken collectively, our data indicate that the acute neuronotoxic actions of BOAA and BMAA (or a metabolite) operate through different glutamate-receptor species. BMAA likely exerts most of its action indirectly via the

A(l) glutamate receptor, while BOAA acts principally at the A(2) and/or A(3) receptor."

Ross, S. M., M. Seelig & P. S. Spencer

1987. Specific antagonism of excitotoxic action of 'uncommon' amino acids assayed in organotypic mouse cortical cultures/ Brain Res. 425:120-127.

Abstr. (adapted): BMAA and BOAA are chemically related excitant amino acids present in the seeds of *Cycas circinalis* and *Lathyrus sativus,* respectively. Consumption of these seeds has been linked to Guam amyotropic lateral sclerosis (BMAA) and lathyrism (BOAA) (a form of primary lateral sclerosis). Authors report that the acute neuronotoxic actions of these amino acids are blocked selectively by specific glutamate receptor antagonists.

Spencer, P. S.

1987. Guam ALS/Parkinsonism-Dementia: A long-latency neurotoxic disorder caused by "slow toxin(s)" in food?/Can. J. Neurol. Sci. (Supp.) 14:347-357.

Abstr.: "Parkinsonism (P) with progressive dementia (D) of the Alzheimer type is recognized as a clinical variant of a form of amyotrophic lateral sclerosis (ALS) that has occurred in high incidence among the Chamorro people of the islands of Guam and Rota in the Marianas chain of Micronesia. The declining annual incidence, upward shifting of the age of onset, narrowing of the sex ratio, and occurrence of the disease among non-Chamorros, point to a disappearing environmental causation peculiar to the traditional culture of these islands. Evidence is presented in support of the proposal that heavy use of certain toxic plants, notably cycad, a traditional source of food and medicine for the Chamorro people, plays an important etiological role. Clinical and epidemiological approaches are offered to test for a relationship between ALS/P-D and plant toxicity."

Spencer, P. S.,M. Ohta & V. S. Palmer

1987. Cycad use and motor neurone disease in Kii Peninsula of Japan/Lancet II (8573): 1462-1463.

During a recent trip through the Kii Peninsula of Honshu Island, Japan, Spencer et al. identified local cases of motor neuron disease in families that commonly use cycads as medicináis. Children may use the seeds as toys. They found that mature seeds of the cycad are stocked in pharmacies in Mie Prefecture, which fill prescriptions requested by local medical practioners.

In Mie Prefecture in October 1987, there were many *Cycas revoluta,* some with large numbers of brilliant red, highly toxic immature seeds. Decades earlier, seeds of this type had been the

playthings of a baby girl who was born and raised in Iseji and who died of motor neuron disease at the age of 25. From babyhood her grandmother had given her each year the red seeds collected from cycads.

For prescriptions from local medicine men the seeds come from Amami Oshima, where detoxified seeds have been used for food and drink when other crops fail due to drought or typhoon and for such ailments as diarrhea, tuberculosis, neuralgia, and to "strengthen the body." This recommendation was found both in Japanese and Chinese folk medicine. Since cycads have provided medicines in tropical and subtropical areas of the world, exposure to cycad products should be considered in studies of the causes of motor neuron diseases and related to neurodegenerative disorders worldwide. Excessive exposure to environmental agents with early onset of neurodegenerative disorders would most likely lead to the rapid identification of relevant etiological factors. Maps of the Japanese area accompany article.

Spencer, P. S., V. S. Palmer, A. Herman & A. Asmedi

1987. Cycad use and motor neurone disease in Irian Jaya. Lancet II (8570): 1273-1274.

Medicinal use of the seed of *C. circinalis* appears to be an etiological factor in the high incidence of ALS and PD in the Pacific area of Guam and Rota in the Mariana Islands and in Irian Jaya in Indonesia. In the present survey, six villages (population 1,200) had five cases of ALS and two of Parkinsonism from 1962 to 1980.

An acceptable remedy, for various skin lesions, used by Auyu villagers, was the scrapings of cycad starch. The poisonous milky exúdate and the sodden mass was applied directly to the lesion on a leaf, then strapped into position until the lesion healed over. Slower increase in the proportion of PD cases reminds one of a similar trend in Guam, where the incidence of ALS has decreased in parallel with a reduction in use of cycad starch for food and medicine.

Spencer, P. S., J. Hugon, A. Ludolph, P. B. Nunn, S. M. Ross, D. N. Roy & H. H. Schaumberg

1987. Discovery and partial characterization of primate motor-system toxins/ In G. Bock & M. O'Connor, eds., Selective Neuronal Death, Wiley, Chicester, Ciba Foundation Symposium 126: 221-238.

From text: "Beta-N-oxalylamino-L-alanine (BOAA) and Beta-N-methylamino-L-alanine (BMAA) are chemically related excitant amino acids isolated from the seed of *Lathyrus sativus* (BOAA) and *Cycas circinalis* (BMAA), consumption of which

has been linked to lathyrism (an upper motor neuron disorder) and Guam amyotrophic lateral sclerosis (ALS), respectively. Both diseases are associated with degeneration of motor neurons. Experimentally, single doses of BOAA or BMAA induce seizures in neonatal mice and postsynaptic neuronal oedema and degeneration in explants of mouse spinal cord and frontal cortex. Preliminary studies show that these behavioural and pathological effects are differentially blocked by glutamate-receptor antagonists. In macaques, several weeks of daily oral doses of BOAA produce clinical and electrophysiological signs of corticospinal dysfunction identical to those seen in comparably well-nourished animals receiving a fortified diet based on seed of *Lathyrus sativus*. By contrast, comparable oral dosing with BMAA precipitates tremor and weakness, bradykinesia and behavioural changes, with conduction deficits in the principal motor pathway. BOAA and BMAA (or a metabolite thereof) are the first members of the excitotoxin family to have been shown to possess chronic motor-system toxic potential. These observations provide a rational basis for searching for comparable endogenous neurotoxins in sporadic and inherited forms of human motor neuron disease."

Spencer, P. S., P. B. Nunn, J. Hugon, A. C. Ludolph, S. M. Ross, D. N. Roy & R. C. Robertson

1987. Guam amyotrophic lateral sclerosis—parkinsonism-dementia linked to a plant excitant neurotoxin/Science 237:517-522.

Abstr.: "The decline in the high incidence of amyotrophic lateral sclerosis, parkinsonism, and Alzheimer-type dementia among the Chamorro population of the western Pacific islands of Guam and Rota, coupled with the absence of demonstrable viral and hereditable factors in this disease, suggests the gradual disappearance of an environmental factor selectively associated with this culture. One candidate is seed of the neurotoxic plant *Cycas circinalis* L., a traditional source of food and medicine which has been used less with the Americanization of the Chamorro people after World War II. Macaques were fed the *Cycas* amino acid beta-N-methylamino-L-alanine, a low-potency convulsant that has excitotoxic activity in mouse brain, which is attenuated by N-methyl-D-aspartate receptor antagonists. These animals developed corticomotoneuronal dysfunction, parkinsonian features, and behavioral anomalies, with chromatolytic and degenerative changes of motor neurons in cerebral cortex and spinal cord. In concert with existing epidemiological and animal data, these findings support the hypothesis that cycad exposure plays an important role in the etiology of the Guam disease."

Spencer, P. S., P. B. Nunn, J. Hugon, A. C. Ludolph, S. M. Ross, D. N. Roy, H. H. Schaumburg & A. I. Soiefer

1987. BMAA and BOAA: Chemically related primate motor neuron toxins isolated respectively from Guamanian *Cycas circinalis* and Indian *Lathyrus sativus*/Presented at Symposium, Anterior Horn Cell Disorders, American Academy of Neurology Scientific Program.

Abstr.: "BMAA is an 'uncommon' amino acid in the seed of *Cycas circinalis* (CC), once used as food on Guam and alleged to cause paralysis, part of the amyotrophic lateral sclerosis Parkinsonian-dementia complex. BMAA is chemically related to BOAA from *Lathyrus sativus* (LS). Daily feeding of macaques with non-convulsive doses of excitatory amino acids from LS and CC seed precipitate[s] disorders of the motor system. The experimental primate disorders elicited by BMAA and BOAA appear to be useful animal models of ALS and lathyrism/LS, respectively. They suggest a new avenue of research on the etiology of ALS on Guam and elsewhere."

Steele, J. C. & T. Guzman

1987. Observations about amyotrophic lateral sclerosis and the parkinsonism-dementia complex of Guam with regard to epidemiology and etiology/Can. J. Neurol. Sci. (Supp.) 14:3 (Aug.).

From abstr.: "For more than 150 years, Chamorro natives of the Mariana Islands in the Western Pacific Ocean, have developed fatal paralysis in middle and later life, which we term amyotrophic lateral sclerosis/parkinsonism-dementia (ALS/ PD). The cause of the disease might be exposure to seeds of the indigenous cycad. Motor system disease is induced in cynomolgus monkeys by feeding them beta-N-methlyamino-L-alanine (BMAA), an amino acid present in cycad seeds. We believe that the cycad seeds which usually cause no immediate adverse symptoms when prepared and eaten as flour, or applied topically as medicine, can give rise to widespread and severe nerve cell degeneration after a latency of many decades. Furthermore, it may be that only a single exposure to this potent but silent toxin(s) can result in fatal neurological disease years later."

Duncan, M., S. Markey & I. Kopin

1988. Letter from National Institutes of Health, Bethesda, Md., to M. G. Whiting, March 31, 1988.

At Natl. Inst. of Mental Health "we have developed a sensitive and precise gas chromatographic/mass spectrometric (GC/MS) assay for the analysis of 2-amino-3-(methylamino)-propionic acid (BMAA). The method allows direct assessment of the BMAA content in food sources and biologic tissues and fluids. The application of GC/MS affords a very high degree of speci-

ficity and the incorporation of a stable isotope standard (deuteromethyl labelled BMAA) allows precise quantification. We can currently detect BMAA in the low picogram/sample range (i.e., < 20 pg) and have confirmed the presence of BMAA in the female gametophyte tissue of the seeds of *Cycas circinalis* L. The seeds of *Cycas revoluta* and *Cycas media* have also been shown to contain BMAA. We have also demonstrated that water washing is effective in removing the neurotoxin BMAA but the amount remaining depends on seed age and the throughness of washing procedure. The quantity of BMAA detected in these seeds is consistent with earlier reports (i.e., ca. 60 mg/100 g wet weight), with considerable variation due to variance in water content of the seed."

Kisby, G. E., D. N. Roy &P. S. Spencer

1988. Determination of beta-N-methylamino-L-alanine (BMAA) in plant *(Cycas circinalis* L.) and animal tissue by precolumn derivatization with 9-fluorenylmethyl chloroformate (FMOC) and reversed-phase high-performance liquid chromatography/ J. Neurosci. Meth. 26:45-54.

Abstr.: A high-performance liquid chromatography (HPLC) method is desribed for determining subpicomole concentrations of beta-N-methylamino-L-alanine (BMAA) in plant and animal tissue. BMAA and other amino acids were reacted with 9-fluorenylmethyl chloroformate (FMOC) for 10 min under alkaline conditions to form highly fluorescent and stable derivatives. All amino acids, including BMAA, eluted from the column within 22 min. BMAA (tr = 18.02 ± 0.07 min) was detected in *Cycas circinalis* L. seed and in serum, cerebrospinal fluid and brain tissue from BMAA-treated monkeys and rats. The primary amino acids glutamine, glutamic acid, aspartic acid, alanine, glycine and gamma-aminobutyric acid (GABA) could also be detected since they were well resolved from BMAA. These amino acids and BMAA were linear over the concentration range of 0.15-7.5 microM with a relative standard deviation ranging from 2.1-6.7%. This method should prove useful in studies to determine the role of BMAA in the Western Pacific amyotrophic lateral sclerosis/Parkinsonism-dementia complex for which cycad seed is the principal etiological candidate.

Norman, L. E.

1988. Cycad toxicity in Guam wild pigs/Field study for M.P.H., School of Public Health, Univ. Hawaii, Honolulu.

Summary: Wild pigs were collected in March 1986 from Anderson Air Force Base in Guam. Brain tissue from the five oldest pigs was examined for histopathological changes. Pigs were

observed consuming cycad plants, but no cycad seeds or plant material was identified in the stomach contents. Local hunters were interviewed.

Most common findings in the wild pigs were extensive parasites (lung worms, kidney worms and intestinal parasites) and liver and kidney lesions deemed to have resulted from the larval migrations. No evidence of cycad toxicity was found.

Parker, C. M.

1988. Dietary history in three villages of Guam prewar and wartime, (1925-1950), with special reference to the role of calcium intake in motor neuron disease/M. S. Thesis in Nutritional Sciences, Univ. Hawaii, Honolulu. 73 p.

Evaluation of the traditional Guamanian diet, which included the use of "fadang," a flour prepared from *Cycas circinalis,* as a food staple when food supplies were reduced.

Weiss, J. H. &D. W. Choi

1988. Beta-N-methylamino-L-alanine neurotoxicity: Requirement for bicarbonate as a cofactor/Science 241:973-975.

From abstr.: "Ingestion of the excitotoxic cycad seed amino acid BMAA may be responsible for the neuronal degeneration associated with Guam ALS-PD in man. However, the basis for the central neurotoxicity of BMAA has been unclear, as it lacks the omega acidic (or equivalent electronegative) moiety characteristic of other excitatory amino acids. BMAA produced neurotoxic and neuroexcitatory effects in murine cortical cell cultures only when physiological concentrations of bicarbonate were available in the extracellular bathing medium. Bicarbonate may interact noncovalently with BMAA to produce, in combination, a molecular configuration that activates glutamate receptors."

Spencer, P. S.

1989. Western Pacific ALS-Parkinsonism-Dementia: A model of neuronal aging triggered by environmental toxins. Pp. 133-144. *In* D. B. Calne, D. Crippa, C. Giancarlo, H. Reinhard, eds. Parkinsonism and Aging, Raven Press, Ltd., N. Y. (In press).

COMMON VERNACULAR NAMES

Family/Genus	*Area*	*Vernacular*
CYCADACEAE		
Cycas		
	Guam	fadang, federico
	Yap	fallutier, faltar, faltir, fratel, Fretel
	Palau	rumi yan
	Nukuoro	manu ata papo
	Fiji	rora, tua wa wa nie
	Australia	bun jinoo, kimalo, nagwiama, zamia palm
	Indonesia	pakis adji, pakis laut, hin-doo-varen
	Malaya	puku gala, todda maram
	India	madan akamapu, wara guda
	Thailand	prong
	Burma	mu dang
	Indochina and China	phong nhi thao, prong te koe, tiek chieu, wu lou tzu, su tieh, hai-te-koe, feng wai tsao
	Japan	sotetsu, tessio
	Ryukyu Islands	nari, yanabu
	Philippine Islands	bitogo, oliva, pitogo
STANGERIACEAE		
Stangeria		
	Madagascar	batsimi saraka, faho, fato, fatra, fatzon, faux sagou tier, samble, tsambou, voa fako, vofaho
ZAMIACEAE		
Lepidozamia		
Macrozamia		
	Australia	arumba, banga, baven, burrawang, kammama, mara, nijar, palm, tchalli, wild pineapple, zamia (seeds: baio, boyar, byyu) black fellows' potatoes, channing nut, kangaroo nut

Encephalartos		
	Africa	bears' nuts, brood boom, caffre bread, ghost's palm, hosannah palm, hottentot's head, kaffir bread, kpadei atah, mam pon mere, mod jajes, nm cusa, wild date
Dioon		
	Mexico	cabeza de chamal, chamal, coyolillo, jango, palma de dolores, palma de la virgen, palma de macetas, sotol, tio tamal
	Honduras	teo sinte
Microcycas		
	Cuba	palma corcho
Ceratozamia		
	Central America	costilla de leon, horned zamia, palma
Zamia		
	Florida	coontie, koontie
	Dominican Republic	guayiga
	Jamaica	sato
	Cuba	palma alcenfor, palma sagu, yuquilla (de ratón)
	Puerto Rico	acesiva, malunguey
	Ecuador	palma de goma
Bowenia		
	Australia	baio, by field fern, fern nuts, gun yoo, jul bin, kug moon ah, ricket fern, zamia fern

SELECTED SUBJECT INDEX

Dossaji et al. 1972; Egoff 1977; Gifford 1946; Goodale 1971; Haring 1952; Harvey 1945; Hirono et al. 1970; Inman 1967; Kurland 1964; Merrill 1943; Miller 1966; Mugera et al. 1968; Parker 1988; Quisumbing 1951; Robertson 1960; Safford 1905; Seawright 1982; Spencer 1987; Spencer, Nunn et al. 1987; Spencer, Palmer et al. 1987; Teruya 1956; Theiret 1958; Thompson 1941; Togashi 1977; Watt et al. 1962; Yokoi 1974.

Toxicity to Animals (Symptoms/Lameness/Death)

Alien 1943; Altenkirk 1974; Anderson et al. 1964; Anon. 1963; Austwick 1962; Bailey 1897; Beatón 1977; Blohm 1962; Britton et al. 1925; Cameron 1909; Campbell 1964; Campbell et al. 1965; Clark 1922-27; Crawley 1898; Dastur et al. 1964; Edwards 1894; Ewart et al. 1909; Gabbedy et al. 1975; Gardiner 1970; Gardner et al. 1956; Gifford 1912, 1946; Hall 1954, 1956, 1957, 1964, 1987; Hernández 1963; Hirono et al. 1969; Holz 1970; Hooper 1978; Hooper et al. 1974; Hurst 1942; Innés et al. 1964, 1965; Juritz 1914; Kono et al. 1985; Lamb 1895; Levene et al. 1964; Maiden 1899a, 1899b; Marks 1912; Mason et al. 1968; Merrill 1943; Miller 1966; Morton 1967; Mugera et al. 1968; Norman 1988; O'Gara et al. 1972; Polsky et al. 1972; Ricourt y Regus 1947; Roberts 1941; Safford 1905; Sanger et al. 1967, 1969; Seawright 1982; Seddon 1930; Spencer, Nunn et al. 1986; Spencer, Ohta et al. 1987; Standley 1920; Standley et al. 1958; Stewart 1899; Steyne et al. 1948; Theiret 1958; Turner 1893; Van Dongen 1903; Vega et al. 1967; Wesley-Smith 1973; Whiting 1963; Yang et al. 1966, 1968; Yasuda et al. 1985; Zellermayer 1969.

Toxicity to Human Beings Via Foods/Incidental Contact

Alien 1943; Anon 1916, 1957, 1960; Beatón 1977, 1982; Beck 1985; Calne et al. 1986; Cleland et al. 1963; Corte y Ruano Calderón 1875; de Freycinet 1829; Dossaji et al. 1972; Fosburg 1956; Hall 1987; Hardin et al. 1969; Haring 1952; Hirono 1972; Hirono et al. 1970; Juritz 1914; Kobayashi 1972; Kurland 1964, 1972; Kurland et al. 1982; Maiden 1899a; Meehan et al. 1977; Merrill 1943; Miller 1966; Morton 1967; Moya et al. 1957; Mugera et al. 1968; Ochse et al. 1931; Parker 1988; Seawright 1982; Spencer 1987; Spencer, Nunn et al. 1986, 1987; Spencer, Nunn, Hugon et al. 1987; Standley et al. 1958; Steele et al. 1987; Steyne et al. 1947; Teruya 1956; Theiret 1958; Turner 1893; Van Dongen 1903; Whiting 1963; Yang et al. 1968.

Assorted Nonfood Uses

Basedow 1925; Hall et al. 1968; Haring 1952; Kobayashi 1955, 1972; Nishida 1934; Spencer, Ohta et al. 1987.

Medicinal

Alien 1943; Anderson 1963; Burkill 1935; Drury 1873; Jackson 1864; Nishida 1934; Quisumbing 1951; Ricourt y Regus 1947; Seawright 1982; Spencer, Ohta et al. 1987; Spencer, Palmer et al. 1987; Standley 1920; Steele et al. 1987; Webb 1960; Whiting 1963.

Composition (Chemical/Nutritional)

Fysh et al. 1960; Maiden 1889; Moretti et al. 1981; Navia et al. 1962; Pétrie 1920; Riggs et al. 1967.

Toxic Compounds

Altenkirk 1974; Anon. 1987; Austwick 1962; Beck 1985; Bell et al. 1967; Calne et al. 1986; Cooper 1941; Dossaji et al. 1972, 1973; Duncan et al. 1988; Forgacs 1971; Fosburg 1956; Hirono 1972; Hooper 1978; Kisby et al. 1988; Kobayashi et al. 1964, 1974; Laqueur et al. 1968; Louw 1975; Miller 1964, 1966; Morreti et al. 1981; Nagahama et al. 1964; Nishida 1936c, 1961; Nunn et al. 1987; Polsky et al. 1972; Riggs 1954, 1956, 1965; Ross & Spencer 1987; Ross, Seelig et al. 1987; Seawright 1982; Spencer, Hugon et al. 1986, 1987; Steele et al. 1987; Strong 1965; Vega et al. 1967, 1968; Weiss 1964; Weiss et al. 1968; Wells 1968; Whiting 1963.

Toxicity Studies With Cycad Components

Anderson et al. 1964; Campbell 1964; Campbell et al. 1965; Crawley 1898; Dastur et al. 1964; Ewart et al. 1909; Gabbedy et al. 1975; Gardner et al. 1956; Hall 1956; Hernández 1963; Innés et al. 1964; Lamb 1895; Laqueur et al. 1963; Levene et al. 1964; Mason et al. 1968; Miller 1966; Nishida 1936c; O'Gara et al. 1964; Sanger et al. 1967; Stanton 1966; Stewart 1898; Steyne et al. 1948; Turner 1893; Watt et al. 1962; Wesley-Smith 1973; Yang et al. 1966.

Toxicity Studies With Selected Compounds

Altenkirk 1974; Anon. 1965; Bell et al. 1967; Gardner 1970; Hirono et al. 1967, 1969; Hooper 1978; Kisby et al. 1988; Kobayashi et al. 1974; Kono et al. 1985; Laqueur et al. 1963; Louw et al. 1975; Masón et al. 1968; Miller 1966; O'Gara et al. 1972; Seawright 1982; Silk 1968; Spencer, Hugon et al. 1986, 1987; Spencer, Nunn et al. 1986, 1987; Spencer, Nunn, Hugon et al. 1987; Stanton 1966; Vega et al. 1967, 1968; Yasuda et al. 1985.

Human Neurodegenerative Diseases (Amyotrophic Lateral Sclerosis/ Parkinsonism-Dementia etc.)

Anon. 1965, 1987; Calne et al. 1986; Fosburg 1956; Garruto et al. 1986; Hall et al. 1968; Hirono et al. 1967; Huston et al. 1956; Innés et al. 1964; Kisby et al. 1988; Kobayashi 1972; Kurland 1964, 1972; Kurland et al. 1982; Laqueur 1977; Laqueur et al. 1963; Lewin 1987; Miller 1966; Nunn et al. 1987; O'Gara et al. 1972; Ross & Spencer 1987; Ross, Seelig et al. 1987; Sanger et al. 1967; Sokoloff 1962; Spencer 1987, 1989; Spencer, Hugon et al. 1986, 1987; Spencer, Nunn et al. 1986, 1987; Spencer, Palmer et al. 1987; Spencer, Nunn, Hugon et al. 1987; Steele et al. 1987; Tustin 1974; Van Houten 1974; Weiss et al. 1988; Whiting 1963, 1964.

Significant Reports/Studies

Anon. 1987; Beatón 1977, 1982; Chamberlain 1919; Kingsbury 1964; Laqueur 1977; Meehan et al. 1977; Murdock et al. 1983; Safford 1905; Spencer, Nunn et al. 1986, 1987; Thompson 1941.

Historical (Society/Government/Religion)

Beatón 1977, 1982; Beck 1985; Carson 1898; Cleland et al. 1963; Coe 1898; Corte y Ruano Calderón 1875; Cox 1904; de Freycinet 1829; Hall 1987; Lamb 1895; Morton 1967; Murdock et al. 1983; Thompson 1941; Villalobos 1833; Zellermayer 1969.

Aborigines

Anderson 1963; Anon. 1916; Beatón 1977, 1982; Beck 1985; Calne et al. 1986; Gardner et al. 1956; Hall 1987; Harvey 1945; Meehan et al. 1978; Murdock et al. 1983; Safford 1905; Turner 1893; Webb 1960.

Reviews/Dictionaries

Burkill 1935; Hurst 1942; Ibanez del Carmen 1865; Jackson 1864; Seawright 1982; Seddon 1930, Theiret 1958; Whiting 1963.

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